EPA Registration Number

89285-1

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

December 3, 2013

Isagro USA, Inc.
c/o Amy Plato Roberts
Technology Sciences Group, Inc.
712 Fifth St., Suite A
Davis, CA 95616

Subject: Application for Minor Formulation Notification to add producers for the basic formulation Confidential Statement of Formula (CSF).
IR9804
EPA Reg. No.: 89285-1
Your submission dated October 14, 2013
Decision Number: 484000

Dear Ms. Roberts:

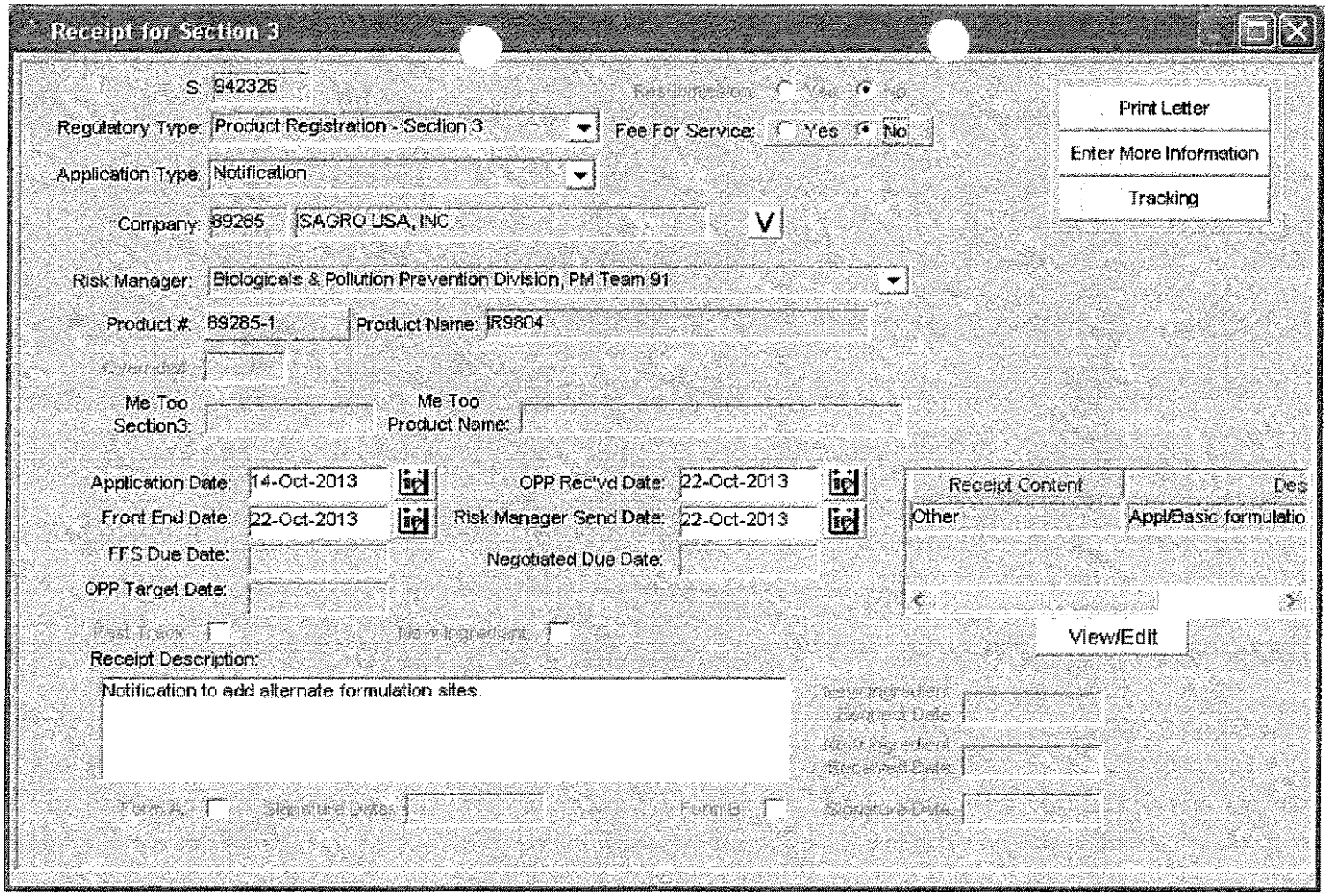
The Biopesticides and Pollution Prevention Division is in receipt of your application for Notification under PR Notice 98-10 dated above. A preliminary screen of this request has been conducted for its applicability under PR Notice 98-10 and it has been determined that the action requested falls within the scope of PR Notice 98-10. Our records have been duly noted and the application submitted has been stamped "Notification Accepted". The acceptable basic formulation CSF dated October 14, 2013 and stamped application will be placed accordingly in our records. The acceptable basic formulation CSF dated October 14, 2013 supersedes all previous acceptable basic formulation CSFs.

If you have any questions concerning this action, please feel free to contact Mr. Colin Walsh at (703) 308-0298 or via email at walsh.colin@epa.gov.

Sincerely,

Linda A. Hollis

Linda A. Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention
Division (7511P)



Decis# 484000

Rec'd
10/23/13
AVB

Please read instructions on reverse side before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA	United States Environmental Protection Agency Washington, DC 20460	☐ Registration ☐ Amendment ☒ Other	OPP Identifier Number

Application for Pesticide – Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
89285-1	**Linda Hollis**	☒ None ☐ Restricted
4. Company/Product (Name) **IRF9804**	PM# **91/Biochemical/BPPD**	

5. Name And Address Of Applicant *(Include ZIP Code)*

Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

☐ *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section II

☐ Amendment – Explain below.
☐ Resubmission in response to Agency letter dated _____
☒ Notification – Explain below.
☐ Final Printed labels in response to Agency letter dated _____
☐ "Me Too" Application.
☐ Other – Explain Below.

Notification Accepted

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Notification to add alternate formulation sites.

Date: DEC 0 3 2013

Reviewer: C. Walsh

This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46, and no other changes have been made to the labeling or the confidential statement of formula for this product. I understand that it is a violation of 18 U.S.C. Sec. 1001 to willfully make any false statement to EPA. I further understand that if this notification is not consistent with the terms of PR Notice 98-10 and 40 CFR 152.46, this product may be in violation of FIFRA and I may be subject to enforcement action and penalties under sections 12

Section III

1. Material This Product Will Be Packaged In:

Child Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☒ No	☐ Yes ☒ No	☐ Yes ☒ No	☒ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) _____
***Certification must be submitted**	If "Yes" Unit Packaging wgt. / No. per Container	If "Yes" Unit Packaging wgt. / No. per Container	

3. Location of Net Contents Information	4. Size(S) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	40 – 168 gallons	☒ On Label ☐ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☒ Lithographed ☐ Pager glued ☐ Stenciled ☐ Other _____

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Mel Graben / mgraben@isagro-usa.com	**Regulatory Manager**	**(919) 321-5203**

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature	3. Title	
	**Regulatory Consultant / aroberts@tsgusa.com**	
4. Typed Name **Amy Plato Roberts**	5. Date **October 14, 2013**	

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete

Material Sent for Data Extraction

Reg. # 89285-1

Description: New Registration

☐ Material(s) Sent to Data Extraction Contractors:

- ☒ New Stamped Label Dated 9/26/13
- ☐ Notification Dated _____
- ☐ New CSF(s) Dated _____
- ☐ Other: _____

☐ Decision #: _____

☐ Other Action/Comments: _____

_____

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Gina Burnett

Phone: 703 605 0513 Division: BPPD

Date: 9/30/2013

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division (7511P)
1200 Pennsylvania Avenue NW
Washington, DC 20460

EPA Reg. Number:	Date of Issuance:
89285-1	

Term of Issuance: **Unconditional**

Name of Pesticide Product:

IR9804

NOTICE OF PESTICIDE:

X Registration

___ Reregistration
(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Amy Plato Roberts
Isagro USA, Inc
P.O. Box 990
Halley, ID 83333

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Biopesticides and Pollution Prevention Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This registration does not eliminate the need for continual reassessment of the pesticide. If EPA determines at any time that additional data are required to maintain in effect an existing registration, the Agency will require submission of such data under section 3(c)(2)(B) of FIFRA. This product is unconditionally registered in accordance with FIFRA Sec. 3(c)(5) provided you:

1. Submit and/or cite all data required for registration of your product under FIFRA section 3(c)(5) when the Agency requires all registrants of similar products to submit such data.

2. Revise the EPA Registration Number to read, "EPA Reg. No. 89285-1."

3. Submit two (2) copies of the final printed labeling before you release the product for shipment. Refer to the A-79 enclosure for a further description of final printed labeling.

A stamped copy of the label is enclosed for your records.

Signature of Approving Official:

Robert McNally, Director,
Biopesticides and Pollution Prevention Division

Date: 9/26/13

EPA Form 8570-6

IR9804

Soil Treatment Pesticide for Formulating Purposes Only

ACTIVE INGREDIENT :
Allyl isothiocyanate (CAS No. 57-06-7)* 99.8%
OTHER INGREDIENTS : 0.2%
TOTAL: 100.0%
*This product contains 8.5 lbs. active ingredient per gallon.

ACCEPTED

SEP 26 2013

Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 89285-1

KEEP OUT OF REACH OF CHILDREN
DANGER — PELIGRO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label find someone to explain it to you in detail.)

FIRST AID	
IF INHALED	· Move person to fresh air. · If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth, if possible. · Call a poison control center or doctor for further treatment advice.
IF IN EYES	· Hold eye open and rinse slowly and gently with water for 15 to 20 minutes. · Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. · Call a poison control center or doctor for treatment advice.
IF ON SKIN OR CLOTHING	· Take off contaminated clothing. · Rinse skin immediately with plenty of water for 15 to 20 minutes. · Call a poison control center or doctor for treatment advice.
IF SWALLOWED	· Call a poison control center or doctor immediately for treatment advice. · Have person sip a glass of water if able to swallow. · Do not induce vomiting unless told to do so by a poison control center or doctor. · Do not give anything by mouth to an unconscious person.
NOTE TO PHYSICIAN: Because rapid absorption may occur through lungs if product is aspirated and cause systemic effects, the decision to induce vomiting or not should be made by a physician.	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. **For Chemical Emergency** **Spill Leak Fire Exposure or Accident** **Call CHEMTREC Day or Night** **Domestic North America 800-424-9300** **International 703-527-3883 (collect calls accepted)**	

EPA Registration No.: (pending as File Symbol 89285-R)
EPA Establishment No.: XXXXXX

NET CONTENTS:

Isagro USA, Inc.
430 Davis Drive, Suite 240, Morrisville, NC 27560

BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Oil of Mustard and Ally Isothiocyanate (AITC)

PC Code: 004901

U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division

(last updated September 26, 2013)

Table of Contents

BIOPESTICIDES REGISTRATION ACTION DOCUMENT (BRAD) TEAM

Branch Chief
Linda A. Hollis, M.S.

Product Chemistry/Human Health Effects/Nontarget Organisms
Russell Jones, Ph.D., Senior Scientist

Regulatory Action Leader
Gina Burnett, M.S.

I. EXECUTIVE SUMMARY

Allyl isothiocyanate (AITC) is a naturally occurring component of Oil of Mustard, which was first registered by the Agency for pesticidal use in 1962. As part of Oil of Mustard, AITC has been determined by the Agency to be the residue of concern and, as such, has been well characterized in the Reregistration Eligibility Decision for Flower and Vegetable Oils (EPA, 1993), the Biopesticides Registration Action Document for Oriental Mustard Seed (PC Code 014921) (EPA, 2008), and the Vegetable and Flower Oil Summary Document for Registration Review (EPA, 2010). AITC is produced naturally when enzymes of the mustard plant, myrosinase and glucosolinate, are in the presence of water. In addition to its presence in mustard, AITC can be found in food commodities such as cooked cabbage, kale, and horseradish. It is synthetically produced from allyl iodide and potassium thiocyanate. In pesticidal products, AITC is used as an insect and animal repellent, feeding suppressant, insecticide, fungicide, herbicide and nematicide.

The Agency has registered the manufacturing-use product (MP), IR9804 (EPA Reg. No. 89285-1) and end-use product (EP), IRF135 (EPA Reg. No. 89285-2). These products contain synthetic AITC at 99.8% and 96.3%, respectively. IRF135 is intended for use as an insecticide, fungicide, herbicide and nematicide to be applied (1) by tractor mounted shank injection at a depth of 8 to 15 inches, followed by tarp overlay, (2) by drip injection, also covered by tarp overlay, and (3) by deep injection to depths greater than 17 inches, with no tarp covering. This is the first proposed soil fumigant containing AITC as its active ingredient. IR9804 is intended for formulation into end-use products for soil treatment. The label application methods are for pre-plant applications, which are considered as non-food uses. No residual activity is expected and the active ingredient and its degredates will dissipate prior to crop seeding.

The Agency has concluded that adequate mammalian toxicology data are available to support AITC (EPA, 1993; EPA 2010). The oral LD_{50} in rats is 339 mg/kg (EPA, 1993). Human exposure to AITC is expected to be minimal from the proposed MP and soil treatment EP, IR9804 (EPA Reg. No. 89285-1) and IRF135 (EPA Reg. No. 89285-2) (EPA, 2013). The active ingredient is not likely to result in adverse human health effects, based upon available reports and information.

AITC rapidly degrades in the environment by normal biological, physical and/or chemical processes that can be reasonably expected to exist where the pesticide is applied (EPA, 2013). In each case of registration of products containing AITC, sufficient data or information has been submitted to demonstrate that there will be no toxicity or adverse effects to nontarget organisms with the exception of certain insects and honey bees (EPA, 2008). The Agency has concluded that the honey bee toxicity issue can be appropriately addressed thru end-use product label mitigation.

On October 1, 2009, the U.S. Environmental Protection Agency (EPA or the Agency) announced a policy to provide a more meaningful opportunity for the public to participate in major registration decisions before they occur. According to this policy, EPA provides a public comment period prior to making a registration decision for the following types of applications: new active ingredients; first food uses; first outdoor uses; first residential uses; or any other

registration actions for which EPA believes there may be significant public interest.

Consistent with the policy of making registration decisions more transparent, the public was provided 15 days in which to submit comments to the Agency regarding its pending decision to register products containing AITC for use as a pre-plant soil treatment. The following documents are available for comment in the docket, identification number EPA-HQ-OPP-2013-0658: a draft of this Biopesticides Registration Action Document (BRAD), the draft product labels for IR9804 (EPA Reg. No. 89285-1) and IRF135 (EPA Reg. No. 89285-2), and the Agency science review memorandum for these products (EPA, 2013). The public participation comment period was open from September 11, 2013 – September 25, 2013. No comments were received during this period.

Following the public participation comment period, the draft BRAD was updated to include additional information on AITC degredates and the draft product label for IRF135 (EPA Reg. No. 89285-2) was revised to include: 1) a five day entry restricted period, 2) directions on notification/sign posting before application, 3) clarification of methods to determine soil and weather conditions, and 4) a table of contents.

The Agency determined that a fumigant management plan, as required for conventional pesticide soil fumigant, is not required for IRF135 (EPA Reg. No. 89285-2) since AITC is not a restricted use pesticide, and all hazards will be mitigated by the personal protective equipment, restricted entry period, and notification requirements included on the product label.

Altogether, the Agency believes that, based on the existing information in the Agency's database on AITC and the recent information submitted in support of the registration of pesticide products containing AITC for pre-plant soil treatment, it is in the best interest of the public to issue the registrations for IR9804 (EPA Reg. No. 89285-1) and IRF135 (EPA Reg. No. 89285-2). The basis for this decision can be found in the science review memorandums for these products (EPA, 2013a; EPA 2013b) and the existing information in the Agency's database on AITC, all of which are characterized in this BRAD.

For definitions of scientific terms, please refer to *http://www.epa.gov/pesticides/glossary/*.

II. ACTIVE INGREDIENT OVERVIEW

Common Name:	Oil of Mustard
Chemical Names:	1-Propene, 3-isothiocyanato- 2-Propenyl isothiochyanate 3-Isothiocyanato-1-propene Allyl isosulfocyanate Allyl isothiocyanate Allyl mustard oil
Trade & Other Names:	Oil of Mustard Allyl isothiocyanate (AITC)
CAS Registry Number:	57-06-7
OPP Chemical Code:	004901
Type of Pesticide:	Biochemical Pesticide – insect and animal repellent, feeding suppressant, insecticide, fungicide, herbicide and nematicide

Biochemical Classification

Oil of Mustard, containing the residue of concern AITC, was first approved by the Agency for use in a registered product as a biochemical insecticide in 1962. For more information regarding product chemistry data requirements, please refer to Tables 1 thru 4 in Appendix A for this document.

III. REGULATORY BACKGROUND

A. Application for Pesticide Registration

On August 29, 2012, Technology Sciences Group, Inc., on behalf of Isagro USA, Inc. (hereafter referred to as "Isagro" or "applicant"), 430 Davis Drive, Suite 240, Morrisville, NC, 27560, submitted applications to register a new biochemical pesticide products, IR9804 (EPA Reg. No. 89285-1) and IRF135 (EPA Reg. No. 89285-2), containing AITC as their active ingredient. IRF135 is intended for use as an insecticide, fungicide, herbicide and nematicide to be applied to be applied (1) by tractor mounted shank injection at a depth of 8 to 15 inches, followed by tarp overlay, (2) by drip injection, also covered by tarp overlay, and 3) by deep injection to depths greater than 17 inches, with no tarp covering. IR9804 is intended for formulation into end-use products for soil treatment.

B. Food Clearances/Tolerances

AITC is exempt from the requirement of a tolerance as stated at 40 CFR § 180.1167:

> **40 CFR § 180.1167 Allyl isothiocyanate as a component of food grade oil of mustard; exemption from the requirement of a tolerance.**
>
> The insecticide and repellent Allyl isothiocyanate is exempt from the requirement of a tolerance for residues when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling.

The end-use product, IRF135 (EPA Reg. No. 89285-2), is labeled for pre-plant soil application only. The active ingredient (synthetic AITC) and its degradates will dissipate prior to planting. The Agency considers this to be a non-food use and, therefore, a tolerance or exemption from the requirement of a tolerance is not required.

IV. RISK ASSESSMENT

A. Product Analysis Assessment (40 CFR § 158.2030)

Biochemical pesticide product analysis data requirements include product chemistry and composition, analysis and certified limits, and physical and chemical characteristics. Product chemistry and composition data include information about the identity of the active ingredient, the manufacturing process, and discussion of the potential for formation of unintentional ingredients. Analysis and certified limits data include information on analysis of samples and certification of limits. Physical and chemical characteristics data describe basic characteristics of the registered pesticide products, including color, physical state, odor, stability, miscibility, pH, corrosion characteristics, viscosity and density.

All product chemistry data requirements have been satisfied for the active ingredient (Oil of Mustard/AITC) and the proposed products, IR9804 (EPA Reg. No. 89285-1) and IRF135 (EPA Reg. No. 89285-2). Refer to Tables 1 thru 4 in Appendix A for a summary of product chemistry data specific to these products. Refer to the Vegetable and Flower Oil Summary Document for Registration Review (EPA, 2010) for a summary of product chemistry information for Oil of Mustard/AITC.

B. Human Health Assessment

1. Tier I Toxicology

AITC has already been assessed by the Agency and the Agency has concluded that adequate mammalian toxicology data are available to support this biochemical pesticide (EPA, 1993; EPA, 2008; EPA 2010). In addition, adequate mammalian toxicology data and information are available to support registration of IR9804 (EPA Reg. No. 89285-1) and IRF135 (EPA Reg. No. 89285-2). This information is summarized below and listed in Table 5 in Appendix A of this document.

Acute Toxicity for IR9804 (EPA Reg. No. 89285-1) and IRF135 (EPA Reg. No. 89285-2) ***(OCSPP Guideline Nos. 870.1100, 870.1200, 870.1300, 870.2400, 870.2500, and 870.2600; Master Record Identification (MRID) Nos. 488241-03 thru -07):***

The acute oral toxicity in rats for IF9804 (EPA Reg. No. 89285-1), containing 99.8% AITC, is LD_{50} = 425.4 mg/kg. Acute dermal toxicity (rat) is LD_{50} > 200 mg/kg, and acute inhalation toxicity (rat) is LC_{50} > 0.21 mg/L. Therefore, IR9804 (EPA Reg. No. 89285-1) is categorized as Toxicity Category II for acute oral toxicity, acute dermal toxicity, and acute inhalation toxicity. It is categorized as Toxicity Category I for primary eye irritation and primary dermal irritation due to its corrosivity, and is classified as a dermal sensitizer. No hypersensitivity incidents have been reported.

Guideline studies for acute human health toxicity testing were not submitted for the EP, IRF135 (EPA Reg. No. 89285-2). In lieu of Guideline studies, the applicant submitted a request to bridge the acute toxicity data submitted in support of the TGAI/MP (containing 99.8% AITC) to support the acute toxicity data requirements for the EP (containing 96.5% AITC). The Agency has determined this request to be acceptable based upon the substantial similar formulation between these two products.

Subchronic Toxicity, Developmental Toxicity, and Mutagenicity Testing for IR9804 (EPA Reg. No. 89285-1) (Tier I) ***(OCSPP Guideline Nos. 870.3100, 870.3250, 870.3465; 870.3700, 870.5100, 870.5300, 870.5375; MRID No. 48824108):***

A Guideline 90-day oral toxicity study was not submitted. In lieu of a study, the applicant cited a 90-day oral toxicity study conducted by the National Toxicology Program (NTP, 1982) on F344/N rats dosed with 1.5 to 25 mg AITC/kg-body wgt/day, five days per week for 13 weeks which had a No Observed Adverse Effect Level (NOAEL) of 25 mg AITC/kg-body wgt/day, the highest level tested. No mortalities occurred during the course of the study and no treatment-related effects were observed on tissues obtained from the test animals when compared to non-treated controls. There were no differences in body weights between treated animals and non-treated controls (EPA, 2013a).

A Guideline 90-day dermal toxicity study was not submitted. The applicant requested and was granted a waiver based on the fact that the product is not intended for application to human skin and prolonged or repeated dermal contact is not expected when EPs for pre-plant soil treatment are applied in accordance with Agency approved use directions and PPE (for handlers: coveralls worn over long sleeve shirt and long pants, chemical resistant footwear plus socks, chemical resistant gloves, protective eyewear, and an air purifying respirator). Similarly, a Guideline 90-day inhalation toxicity study was not submitted. The applicant requested and was granted a waiver based on the fact that repeated inhalation exposure to AITC aerosol, vapor or gas is highly unlikely and not expected, when the EPs for pre-plant soil treatment is applied in accordance with EPA approved label use directions and PPE.

A Guideline Prenatal Developmental Toxicity study was not submitted. In lieu of a study, the applicant cited a study in which AITC was one of 16 chemically-related compounds evaluated in order to correlate potential developmental toxicity with molecular structure. In this study, no

difference in the percentage of abnormal fetuses in AITC-treated offspring were detected compared to control, and no difference between treated and control in the percentage of dead fetuses was detected. The authors concluded that AITC did not display any teratogenic potential at the NOAEL of 60 mg/kg. The 60 mg/kg dose would be equivalent to 4.2 g AITC for a standard 70 kg human (EPA, 2013a).

Guideline Mutagenicity studies were not submitted. In lieu of a study, the applicant cited a battery of mutagenicity studies on AITC conducted by the National Toxicology Program (NTP). In this battery, two reverse mutation studies confirmed that mutagenicity responses were negative in all strains tested with and without S9 activation. In three *in vitro* mammalian gene mutation studies, a negative response was observed in the first trial using mouse lymphoma cells without S9 activation at concentrations ranging from 0.05 to 0.8 mg/mL AITC. A second trial without S9 exhibited a significant increase in average mutant frequency and significant reduction in relative total growth at AITC concentrations of 0.4, 0.6, and 0.8 mg/mL; 1.0 mg/mL was cytotoxic. A third trial without S9 also exhibited a significant increase in average mutant frequency at concentrations of 0.6 to 1.4 mg/mL and a significant reduction in growth; a concentration of 1.6 mg/mL was cytotoxic. It is noted that the positive results were observed without S9 activation and in the presence of substantial cytotoxicity. An *in vivo* mammalian chromosome aberration study was conducted with mice dosed intraperitoneally with 0, 25, or 50 mg/kg AITC and compared against mice dosed with a positive control, dimethylbenzanthracine (DMBA). Increases in chromosome aberrations were not observed in AITC treated mice when compared to non-treated (negative) controls, while a positive response was observed in DMBA-treated mice. The Agency has determined that the weight of evidence demonstrates that AITC is not likely to be a mutagen. In addition, the method of application and rapid degradation rate for the proposed pre-plant soil treatment, together with appropriate PPE, mitigates exposure to humans (EPA, 2013a).

2. Tier II and Tier III Toxicity Studies

The biochemical pesticide Human Health Assessment data requirements for Tier II and Tier III were not required due to the low toxicity of the active ingredient and the low levels of exposure expected from its intended uses in EP products.

3. Effects on the Endocrine System

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine related effects caused by the substance, and

establish a dose-response relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA issued test orders and data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and nine inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

AITC (as contained in Oil of Mustard) is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders and data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

4. Dose Response Assessment

No toxicological endpoints have been identified for Oil of Mustard or AITC; therefore, a dose-response assessment was not required.

5. Drinking Water Exposure and Risk Characterization

No significant exposure from drinking water is expected when products containing Oil of Mustard or AITC are used according to the product label directions. AITC is a naturally occurring component of the human diet and degrades rapidly in the soil with a short half-life (T½) ranging from 20 to 60 hours. AITC transforms in sterilized soil at the same rate as intact soil, indicating that degredation is not dependent on soil microbial populations. Products containing AITC will not be directly applied to water. However, in an aqueous solution in the pH range between 6 and 8, AITC is proposed to degrade completely. Within this pH range, the primary decomposition products identified were: allyl thiocyanate (ATC); allylamine (AA); and carbon disulfide (CDS). ATC, an isomer of AITC, is expected to completely degrade in soil in approximately 4-5 days post application. The remaining two degradates, AA and CDS are expected to rapidly degrade by microbial activity in the soil in time frames that are much less than 5 days based on the weight of laboratory evidence. Should any amount of AITC or its degradates volatilize into the atmosphere, they will be rapidly diluted and degraded via reaction with photochemically produced hydroxyl radicals (EPA, 2013a; EPA, 2013b).

6. Occupational, Residential, School and Day Care Exposure and Risk Characterization

a. Occupational Exposure and Risk Characterization

Occupational exposure to the proposed soil treatment EP, IRF135 (EPA Reg. No. 89285-2), is not expected due to mitigation through precautionary language and personal protective

equipment (PPE) on the label. For other products containing AITC, the Agency has required labels to include the appropriate signal word and precautionary statements, as PPE if applicable, to mitigate any risk of exposure.

b. Residential, School and Day Care Exposure and Risk Characterization

Soil treatment of the EP, IRF135 (EPA Reg. No. 89285-2), is for agricultural use only. Previously approved AITC products for outdoor residential use have been approved by the Agency based on minimal exposure to AITC when used according to label directions. No indoor residential, school, or day care uses are currently approved for products containing AITC.

7. Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation

There is reasonable certainty of no harm to U.S. populations, including infants and children, from aggregate exposures to residues of AITC when used as proposed. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. Moreover, potential non-occupational inhalation and dermal exposure is not likely to pose any adverse effects to exposed populations via aggregate and cumulative exposure.

a. Food Exposure

Dietary exposure of AITC is already occurring, given that this substance can be found in many foods commonly consumed by humans such as cooked cabbage, kale, horseradish, and mustard. AITC is exempt from the requirement of a tolerance for residues when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling. Furthermore, the proposed use of synthetic AITC as a pre-plant soil treatment will not result on residues on food as the AITC, and its degradates, will readily degrade prior to planting (EPA, 2013a).

b. Drinking Water Exposure

The proposed use of synthetic AITC as a pre-plant soil treatment will not result in water residues because this biochemical degrades rapidly in the soil with a short half-life (T½) ranging from 20 to 60 hours. Products containing AITC will not be directly applied to water. However, in an aqueous solution in the pH range between 6 and 8, AITC is proposed to degrade completely. Therefore, drinking water exposure from the proposed used pattern is not expected to pose incremental risk to adults, infants and children via drinking water consumption.

c. Other Non-occupational Exposure

Soil treatment of the EP, IRF135 (EPA Reg. No. 89285-2), is for agricultural use only. Previously approved AITC products for outdoor residential use have been approved by the Agency based on minimal exposure to AITC when used according to label directions. Other non-occupational use is not expected for products containing this active ingredient.

8. Cumulative Effects from Substances with a Common Mechanism of Toxicity

AITC has no demonstrated subchronic toxicity; thus, there is no reason to expect cumulative effects of exposure to Pear Ester and to other substances with common mechanism of toxicity.

9. Determination of Safety for United States Population, Infants and Children

AITC is exempt from the requirement of a tolerance for residues when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling. Therefore, it is expected that no harm will result from aggregate exposure to the United States population, including infants and children, to the residues of AITC on food commodities. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. Thus, there are not threshold effects of concern and consequently, provisions requiring additional margin of safety do not apply. Furthermore, the use of synthetic AITC as a pre-plant soil treatment will not result on residues on food as the AITC, and its degradates, will readily degrade prior to planting (EPA, 2013a).

10. Risk Characterization

The Agency considered human exposure to AITC in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the use of products containing AITC when label instructions are followed.

C. Environmental Assessment

1. Ecological Hazards

Oil of Mustard and AITC have already been assessed by the Agency and the Agency has concluded that adequate nontarget organism toxicology data and information are available to support these ingredients (EPA, 1993; EPA, 2008; EPA 2010). In addition, adequate nontarget organism toxicology data information were to support registration of IR9804 (EPA Reg. No. 89285-1) and IRF135 (EPA Reg. No. 89285-2). This information is summarized in Table 6, in Appendix A of this document.

2. Environmental Fate and Ground Water Data

Environmental fate and groundwater data are not required at this time because the results of the nontarget organism toxicity assessment (Tier I data requirements) did not trigger these Tier II data requirements.

3. Ecological Exposure and Risk Characterization

Exposure and risk from the registered and proposed (pre-plant soil treatment) uses of AITC are expected to be minimal for nontarget organisms, with the exception of honey bees (EPA, 2013a). Exposure to honey bees will be mitigated by appropriate label language on end-use products.

4. Endangered Species Assessment

The Agency believes that Oil of Mustard and AITC will have "No Effect" on any currently listed threatened and endangered species, or any designated critical habitat, as listed by the U.S. Fish and Wildlife Service (USFWS) and the National Oceanic and Atmospheric Administration's (NOAA) National Marine Fisheries Service (NMFS) (EPA, 2010). EPA anticipates conducting no further analysis of potential risks to endangered or threatened species unless public comments during the Registration Review process alter the Agency's current position. The Registration Review for these active ingredients is ongoing as of the date of this document, September, 2013.

D. Product Performance Data

Product performance (efficacy) data must be developed for all pesticides to ensure that the products will perform as intended and that unnecessary pesticide exposure to the environment will not occur as a result of the use of ineffective products. The Agency reserves the right to require, on a case-by- case basis, the submission of efficacy data for any pesticide product registered or proposed for registration, but applications to register pesticide products intended to control a pest of significance public health importance, as defined in FIFRA section 28(d) and section 2(nn), must include such data. For further guidance on the product performance data requirement, refer to Pesticide Registration Notice (PR) Notices 96-7, 2002-1 and Explanation of Statutory Framework for Risk-Benefit Balancing for Public Health Pesticides (http://www.epa.gov/PR_Notices/pr1996-7.pdf) (http://www.ea.gov/PR_Notices/pr2002-1.pdf) and (http://www.epa.gov/pesticides/health/risk-benefit.htm).

Oil of Mustard and AITC are not intended to be formulated into products to control public health pests as defined in FIFRA section 28(d) and section 2(nn), and product performance (efficacy) was not evaluated by the Agency.

V. RISK MANAGEMENT DECISION

A. Determination of Eligibility for Registration

Section 3(c)(5) of FIFRA provides for pesticide product registration if it is determined that: (A) its composition warrants proposed claims; (B) its labeling and other materials comply with the requirements of FIFRA; (C) it will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice, it will not generally cause unreasonable adverse effects on the environment.

The four eligibility criteria have been satisfied for the proposed pesticide products containing the active ingredient AITC (and for all previous registered pesticide products containing AITC and Oil of Mustard).

B. Regulatory Decision

The data submitted fulfill the requirements for the unconditional registration IR9804 (EPA Reg. No. 89285-1) as an MP to be formulated into soil treatment products and IRF135 (EPA Reg. No.

89285-2) as an EP for pre-plant soil treatment. EPA is granting these unconditional registrations. For these product labels and for product-specific labels and information on other product containing Oil of Mustard and AITC, please refer to http://www.epa.gov/pesticides/pestlabels.

C. Environmental Justice

EPA seeks to achieve environmental justice—the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income—with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies. At this time, EPA does not believe that products containing the active ingredients Oil of Mustard or AITC, or the use of AITC for pre-plant soil treatment will cause harm or a disproportionate impact on at-risk communities. For additional information regarding environmental justice issues, please visit EPA's website at *http://www.epa.gov/compliance/environmentaljustice/index.html*.

VI. ACTIONS REQUIRED BY REGISTRANTS

EPA evaluated all data submitted in connection with the registration of AITC for pre-plant soil treatment and determined that these data are sufficient to satisfy current registration data requirements. At this time, no additional data must be submitted to EPA for these particular products. For new uses and/or changes to existing uses, EPA may require additional data. Notwithstanding the information stated in the previous paragraph, it should be clearly understood that certain specific data are required to be reported to EPA as a requirement for maintaining the federal registration for a pesticide product. A brief summary of these types of data are listed below.

A. Reporting of Adverse Effects

Pursuant to FIFRA section 6(a)(2), reports of all incidents of adverse effects to the environment must be submitted to EPA.

B. Reporting of Hypersensitivity Incidents

Under the provisions of 40 CFR Part 158.2050(d), all incidents of hypersensitivity (including both suspected and confirmed incidents) must be reported to the Agency.

VII. Appendix A. Data Requirements (40 CFR Part 158-Subpart U)

TABLE 1. Product Chemistry Data Requirements for IR9804 (99.8% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Study**	**Results**	**MRID**
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Submitted data satisfy the requirements for product identity, manufacturing process, and discussion of formation of impurities. **ACCEPTABLE**	48824101
830.1700	Analysis of samples	Submitted data satisfy the requirements for analysis of samples. **ACCEPTABLE**	48824102
830.1750	Certification of limits	Limits listed in the CSF are **ACCEPTABLE**	-
830.1800	Analytical method	**ACCEPTABLE**	48824102

TABLE 2. Physical and Chemical Properties of IR9804 (99.8% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result**	**MRID**
830.6302	Color	Colorless or pale yellow liquid	48824101
830.6303	Physical State	Liquid	48824101
830.6304	Odor	Very pungent, irritating aroma	48824101
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Reported stable.	48824101
830.6315	Flammability	Flashpoint = 46°C	48824101
830.6317	Storage Stability	Study in progress – anticipated completion date is the last quarter of 2013.	48824101
830.6319	Miscibility	Not Applicable; TGAI/MP is not an emulsifiable liquid and is not diluted with petroleum solvents.	-
830.6320	Corrosion Characteristics	Study in progress – anticipated completion date is the last quarter of 2013.	48824101
830.7000	pH	4-5	48824101
830.7050	UV/Visible Light Absorption	Refractive index 1.524-1.531; see http://www.fao.org/ag/agn/jefca-flav/img/img/1560.gif for the absorbance spectrum	48824101
830.7100	Viscosity	Not Applicable for TGAI/MP	-
830.7200	Melting Point/Range	-102.5°C	48824101
830.7220	Boiling Point/Range	150-151°C; 148-154°C	48824101
830.7300	Density	1.013-1.020; 1.0	48824101
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not Applicable; TGAI/MP is not fibrous	-
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Log P = 2.11	48824101
830.7840	Water Solubility	Slightly soluble in water	48824101
830.7950	Vapor Pressure	1.33 kPa @ 38.3°C 0.493 kPa@ 20°C	48824101

TABLE 3. Product Chemistry Data Requirements for IRF135 (96.3% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Study**	**Results**	**MRID Method/Reference**
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Submitted data satisfy the requirements for product identity, manufacturing process, and discussion of formation of impurities. **ACCEPTABLE**	489194-01
830.1700	Analysis of samples	Not required for EP	489194-02
830.1750	Certification of limits	Limits listed in the CSF are **ACCEPTABLE**	489194-01
830.1800	Analytical method	Not required for EP	489194-02

TABLE 4. Physical and Chemical Properties of IRF135 (96.3% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result**	**MRID**
830.6302	Color	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6303	Physical State	Liquid	489194-01
830.6304	Odor	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6315	Flammability (flashpoint)	47°C	489194-02
830.6317	Storage Stability	Study in progress– anticipated completion date is the last quarter of 2013.	489194-01
830.6319	Miscibility	Not applicable per 40 CFR 158.2030(e)(10) – EP is not an emulsifiable liquid and is not to be diluted with petroleum solvents.	-
830.6320	Corrosion Characteristics	Study in progress– anticipated completion date is the last quarter of 2013.	489194-01
830.7000	pH	4.87 (1% soln)	489194-02
830.7050	UV/Visible Light Absorption	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7100	Viscosity	0.6 centistokes @ 40°C 0.8 centistokes @ 20°C	489194-02
830.7200	Melting Point/Range	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7220	Boiling Point/Range	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7300	Density	1.019 g/mL @ 20°C	489194-02
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7840	Water Solubility	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7950	Vapor Pressure	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-

Table 5. Mammalian Toxicology Data Requirements for IR9804 (EPA Reg. No. 89285-1) (40 CFR § 158.2050)			
Study/OPPTS Guideline No.	Results	Toxicity Category/Description	MRID
Acute oral toxicity (rat) (870.1100)	LD_{50} = 425.4 mg/kg **ACCEPTABLE**	II	488241-03
Acute dermal toxicity (rat) (870.1200)	LD_{50} > 200 mg/kg **ACCEPTABLE**	II	488241-04
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 0.21 mg/L **ACCEPTABLE**	II	488241-05
Primary eye irritation (rabbit) (870.2400)	Waiver due to observed corrosiveness on skin **ACCEPTABLE**	I	1
Primary dermal irritation (rabbit) (870.2500)	Corrosive **ACCEPTABLE**	I	488241-06
Dermal sensitization (guinea pig) (870.2600)	Sensitizer **ACCEPTABLE**	-	488241-07
Hypersensitivity incidents (885.3400)	-	-	-
90-Day oral toxicity (870.3100)	Rationale submitted **ACCEPTABLE**		488241-08
90-Day dermal toxicity (870.3250)	Rationale submitted **ACCEPTABLE**		488241-08
90-Day inhalation toxicity (870.3465)	Rationale submitted **ACCEPTABLE**		488241-08
Mutagenicity (870.5100, 5300 and 5375)	Rationale submitted **ACCEPTABLE**		488241-08
Developmental toxicity (870.3700)	Rationale submitted **ACCEPTABLE**		488241-08

Table 6. Non-Target Organism Data Requirements for IR9804 (EPA Reg. No. 89285-1) (40 CFR § 158.2060)			
Study/OPPTS Guideline No.	Results	Toxicity Category/Description	MRID
Avian Acute Oral/OPPTS 850.2100	Rationale submitted **ACCEPTABLE**	No acute oral exposure based on application method and rapid environmental degradation	48824108, p. 18
Avian Dietary/OPPTS 850.2200	Rationale submitted **ACCEPTABLE**	No dietary exposure based on application method and rapid environmental degradation	48824108, p. 20
Freshwater Fish LC50/OPPTS 850.1075	Rationale submitted 96-hr LC_{50} = 0.077 ppm **ACCEPTABLE**	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation	48824108, pp. 22, 37-47
Freshwater Invertebrate/OPPTS 850.1010	Rationale submitted 48-hr EC_{50} = 0.73 ppm **ACCEPTABLE**	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation	48824108, pp. 23, 216-221
Non-target Plants/OPPTS 850.4100 & 4150	Rationale submitted **ACCEPTABLE**	No non-target exposure based on application method and rapid environmental degradation	48824108, pp. 24-27
Non-target Insects	Rationale submitted **ACCEPTABLE**	No non-target exposure based on application method and rapid environmental degradation	48824108, pp. 28, 29

VIII. Appendix B. References

1. U.S. EPA, 1993. Registration Eligibility Decision (RED). Flower and Vegetable Oils. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). December 1, 1993. Available at: http://www.epa.gov/opp00001/chem_search/reg_actions/reregistration/red_G-114_01-Dec-93.pdf

2. U.S. EPA, 2008. Oriental Mustard Seed (PC Code 014921). Biopesticides Registration Action Document. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). December 17, 2008. Available at: http://www.epa.gov/pesticides/chem_search/reg_actions/registration/decision_PC-014921_17-Dec-08.pdf

3. U.S EPA, 2010. Vegetable and Flower Oils Summary Document. Registration Review: Initial Docket. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). March 29, 2010. Available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0904-0005

4. U.S. EPA, 2013a. Memorandum from Russell Jones, Ph.D. to Gina Burnett. Science Review in Support of the Registration of the TGAI/MP IR9804 and the EP, IRF 135, Respectively Containing 99.8% and 96.3% Allyl Isothiocyanate (AITC) As Their Active Ingredient. The TGAI/MP is an unregistered source of the active ingredient. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). May 15, 2013.

5. U.S EPA, 2013b. Memorandum from Russell Jones, Ph.D. to Gina Burnett. Revised Science Review in Support of the Registration of the TGAI/MP IR9804 and the EP, IRF 135, Respectively Containing 99.8% and 96.3% Allyl Isothiocyanate (AITC) As Their Active Ingredient. The TGAI/MP is an unregistered source of the active ingredient. Environmental Fate Addendum. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). September 18, 2013.

IX. GLOSSARY OF ACRONYMS AND ABBREVIATIONS

a.i.	active ingredient
BPPD	Biopesticides and Pollution Prevention Division
BRAD	Biopesticide Registration Action Document
bw	body weight
CBI	Confidential Business Information
CFR	Code of Federal Regulations
cm^3	cubic centimeter
CSF	Confidential Statement of Formula
°C	degrees Celsius
EC_{50}	median effective concentration. A statistically derived single concentration in environmental medium that can be expected to cause an effect in 50% of the test animals when administrated by the route indicated (inhalation). It is expressed as a concentration in air or water (e.g. mg/L).
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EP	end-use product
EPA	Environmental Protection Agency (the "Agency")
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FR	Federal Register
g	gram
ha	hectare
kg	kilogram
Kow	octanol-water partition coefficient
L	liter
LC_{50}	median lethal concentration. A statistically derived single concentration in air or water that can be expected to cause death in 50% of the test animals when administrated by the route indicated (inhalation and environment). It is expressed as a concentration in air or water (e.g. mg/L).
LD_{50}	median lethal dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral and dermal). It is expressed as a weight of substance per unit weight of animal (e.g., mg/kg).
MRID No.	Master Record Identification Number
mg	milligram
mPa	millipascal
mL	milliliter
MP	manufacturing-use product
N/A	not applicable
NE	"No Effect"
NIOSH	National Institute for Occupational Safety and Health

nm	nanometer
NOEL	no-observed-effect-level
NOF	notice of filing
NOR	notice of receipt
OPP	Office of Pesticide Programs
OCSPP	Office of Chemical Safety and Pollution Prevention
pa	pascal
PPE	personal protective equipment
PR Notice	Pesticide Registration Notice
TGAI	technical grade of the active ingredient
ug	microgram
USDA	United States Department of Agriculture
UV	ultra-violet

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F I F R A

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Office of Chemical Safety and Pollution Prevention

MEMORANDUM **September 18, 2013**

SUBJECT: Revised Science Review in Support of the Registration of the TGAI/MP IR9804 and the EP, IRF 135, Respectively Containing 99.8% and 96.3% Allyl Isothiocyanate (AITC) As Their Active Ingredient. The TGAI/MP is an unregistered source of the active ingredient. Environmental Fate Addendum

Decision No :	469288 & 469289
DP Nos.:	406246 & 406248
EPA Reg. Nos:	89285-R & -E
Chemical Class:	Biochemical
CAS. No.:	57-06-7
PC Code:	004901
Tolerance Exemptions :	40 CFR 180.1167 (for AITC) in Oil of Mustard
MRID Nos. :	488241-01 to -08 & 489194-01 to -03

FROM: Russell S. Jones, Ph.D, Senior Biologist /S/ 09/18/2013
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Gina Burnett, Regulatory Action Leader /S/ 09/18/2013
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

In response to a request for additional information and on behalf of Isagro, A. Roberts (TSG) submitted environmental fate data on AITC and its degradates in support of the registration of the TGAI/MP IR9804 and the EP, IRF 135, respectively containing 99.8% and 96.3% Allyl Isothiocyanate (AITC) as their active ingredient. The TGAI/MP is an unregistered source of the active ingredient.

The registrant had previously submitted Product Chemistry and Tier I Toxicity information and waivers for all Tier I Non-Target Organism data requirements which were reviewed and deemed

acceptable (**See Memorandum from R. S. Jones to G. Burnett, dated 05/15/2013**). In an email to A. P. Roberts (TSG, Inc), dated 8/15/2013, the following request for additional information was transmitted by the Agency:

"Management is requesting more information on the sold degradates of AITC (allylamine, carbon disulfide, and ATC) before moving forward with these registrations. Does ISAgro have quantitative information on the half-life of these compounds? And/or is there information availability to demonstrate low or no toxicity?"

In response, A.P. Roberts (TSG, Inc) submitted additional environmental fate information which is contained in a letter (A. P. Roberts to L. Hollis, dated 08/21/2013). Much of this information was submitted in the previous submission.

ENVIRONMENTAL FATE EXECUTIVE SUMMARY

Allylisothiocyanate (AITC) and its major degradates, Allylthiocyanate (ATC), Allylamine (AA), and Carbon disulfide (CDS), are expected to rapidly degrade in soil following application according to proposed label use instructions (tarp covered and deep injected following application). AITC and its structurally similar isomer ATC, with which it readily interconverts, are expected to completely degrade in soil in approximately 4-5 days post application. The remaining two degradates, AA and CDS are expected to rapidly degrade by microbial activity in the soil in time frames that are much less than 5 days based on the weight of laboratory evidence. Should any amount of AITC or its degradates volatilize into the atmosphere, they will be rapidly diluted and degraded via reaction with photochemically produced hydroxyl radicals.

AITC and its major degradates are not expected to be 5 days following application of the end-use product, , IRF 135 (EPA File Symbol No. 89285-E) when applied according to Agency approved label directions.

Details of this Re-evaluation of the Environmental Fate Information begins on page 5 of this document.

SUMMARY OF THE EXISTING STUDIES/DATA/INFORMATION

Under 40 CFR 180.1167 Allyl isothiocyanate is exempt from the requirement of a tolerance for residues when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling. The inert ingredient is cleared for food use under 40 CFR 180.910.

The currently proposed label application methods are for pre-plant applications, which would be considered a non-food use. No residual activity is expected and the active ingredient will dissipate prior to crop seeding (10 days post application according to the draft label).

I. Active Ingredient Characterization (MRID 488241-01 & -02)

Allyl isothiocyanate (AITC) is the major component of natural mustard oil. It is present also in cooked cabbage, horseradish, and black mustard seed. It is synthetically produced from allyl iodide and potassium thiocyanate

Product Names: TGAI/MP: IR9804 (99.8% a.i.) (EPA File Symbol No. 89285-R)
EP: IRF135 (96.3% a.i.) (EPA File Symbol No. 89285-E)

Chemical Name:	Allyl isothiocyanate
Common Names:	AITC, 3-Isothiocyanato-1-propene
PC Code:	070704
CAS No.:	56-06-7
Molecular Wgt.:	99.15
Chemical Formula:	C_4H_5NS

II. Human Health Data Summary

The data presented in Table1 below are a summary of the toxicity data and information submitted to support the TGAI/MP. Data and information submitted in support of the TGAI/MP were bridged to support the EP. Guideline studies for acute toxicity testing were not submitted. In lieu of Guideline studies, the registrant submitted a request to bridge the acute toxicity data submitted in support of the TGAI/MP (containing 99.8% AITC) to support the acute toxicity data requirements for the EP (containing 96.5% AITC) [redacted]

These studies/data were previously reviewed by the Agency and deemed **ACCEPTABLE** (see Memorandum from R. S. Jones to G. Burnett, dated 05/15/2013).

Inert ingredient information may be entitled to confidential treatment

Table 1. Mammalian Toxicology Profile for TGAI/MP AITC (40 CFR § 158.2050)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute oral toxicity (rat) (870.1100)	LD_{50} = 425.4 mg/kg	II	488241-03
Acute dermal toxicity (rat) (870.1200)	LD_{50} > 200 mg/kg	II	488241-04
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 0.21 mg/L	II	488241-05
Primary eye irritation (rabbit) (870.2400)	Waiver due to observed corrosiveness on skin	I	-
Primary dermal irritation (rabbit) (870.2500)	Corrosive	I	488241-06
Dermal sensitization (guinea pig) (870.2600)	Sensitizer	-	488241-07
Hypersensitivity incidents (885.3400)	-	-	-
90-Day oral toxicity (870.3100)	NOAEL = 25 mg AITC/kg bw/day No clinical effects observed	No subchronic toxicity	488241-08
90-Day dermal toxicity (870.3250)	No repeated exposure expected based on application methods and PPE requirements	-	488241-08
90-Day inhalation toxicity (870.3465)	No repeated exposure expected based on application methods and PPE requirements	-	488241-08
Mutagenicity (870.5100, 5300 and 5375)	Not a mutagen based on 3 studies conducted by NTP 1981, 1988, & 1991.	Not a mutagen	488241-08
Developmental toxicity (870.3700)	NOAEL = 60 mg AITC/kg bw/day No clinical effects observed	Not a teratogen	488241-08

III. Nontarget Organism Data Summary

The data presented in Table 2 below are a summary of the nontarget organism toxicity data and information submitted to support of the TGAI/MP. Refer to the appropriate pages in MRID 48844108 for more detailed information and specific reference citations from the scientific literature. These studies/data were previously reviewed by the Agency and deemed **ACCEPTABLE** (see Memorandum from R. S. Jones to G. Burnett, dated 05/15/2013).

Table 2. Non-Target Organism Data Requirements for TGAI/MP AITC (40 CFR § 158.2060)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Avian Acute Oral/OPPTS 850.2100	-	No acute oral exposure based on application method and rapid environmental degradation	48824108, p. 18
Avian Dietary/OPPTS 850.2200	-	No dietary exposure based on application method and rapid environmental degradation	48824108, p. 20
Freshwater Fish LC50/OPPTS 850.1075	96-hr LC_{50} = 0.077 ppm	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation	48824108, pp. 22, 37-47
Freshwater Invertebrate/OPPTS 850.1010	48-hr EC_{50} = 0.73 ppm	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation	48824108, pp. 23, 216-221
Non-target Plants/OPPTS		No non-target exposure based on	48824108, pp. 24-

Table 2. Non-Target Organism Data Requirements for TGAI/MP AITC (40 CFR § 158.2060)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
850.4100 & 4150	-	application method and rapid environmental degradation	27
Non-target Insects	-	No non-target exposure based on application method and rapid environmental degradation	48824108, pp. 28, 29

Guideline studies were not submitted in support of the non-target organism data requirements. In lieu of Guideline studies, the applicant submitted rationales, on a Guideline-by-Guideline basis, for each non-target organism data requirement, which were supported both by scientific literature citations as well as an argument for a lack of exposure to non-target organisms to AITC based on its rapid degradation in soil, its widespread presence in commonly eaten foods, as well as by the methods and timing of application of the EP. These rationales were previously reviewed and deemed **ACCEPTABLE**.

The environmental fate of AITC is discussed in detail below. This information, as well as additional environmental fate information submitted by A. P. Roberts (TSG, Inc.) is re-evaluated here in support of the registrations of TGAI/MP IR9804 and the EP, IRF 135, respectively containing 99.8% and 96.3% Allyl Isothiocyanate (AITC) as their active ingredient.

Re-Evaluation of the Environmental Fate Allyl Isothiocyanate (AITC) a component of Oil of Mustard

A. Proposed Label Use Applications of the End-Use Product

The end-use product is intended to be applied according to the following methods:

1. Tractor-mounted shank injection at a depth of 8-15 inches followed by a tarp overlay;
2. Drip injection covered by a tarp overlay; and
3. Deep injection (>17-inches in depth) with no tarp covering.

Tarps are not to be removed until 5 days post application. Non-tarped, deep injection applications will have soil compacted over the injection line at planting, to prevent any escape of volatiles.

B. Uses of AITC

AITC has many streams into the environment. It may enter the environment indirectly via its use as a flavoring agent, and in pharmaceutical ointments and mustard plasters. AITC enters the environment directly via its use as an animal repellent and as a soil fumigant. It is a

naturally-occurring substance present in the leaves and seeds of *Brassica* Family plants, horse radish, and some cabbages. It is a root exudate of the invasive plant, garlic mustard (*Allaria petiolata*). The general public may be exposed to AITC via ingestion of certain foods and dermal contact with consumer products containing AITC (HSDB, 2013a, Accessed 09/17/2013). The estimated world consumption of allyl isothiocyanate/year is 455,000 and 79,000 kg from direct plant material and synthetic products, respectively (Pechacek et al., 1997 as cited by HSDB, 2013).

C. Fate of Applied Allylisothiocyanate in AITC in Soil & Water

When applied to soil as oil of mustard or as homogenized tissue of Mustard Family plants, sinigrin, the major glucosinolate compound in the plant tissue and oil, is degraded by the action of the enzyme myrosinase in the presence of moisture to yield allylisothiocyanate (AITC).

AITC has been observed to degrade rapidly in soils with a short half-life (T½) ranging from 20 to 60 hours (0.83 to 2.5 days) (Borek et al., 1995). The average T½ of AITC in six different soil types was reported to be 47 ± 27 hours, with the greatest degradation rate of in soils that have high organic carbon and total nitrogen (N) content. In addition, the AITC T½ in soil increases with increasing moisture content and decreases in soil with increasing temperature between 10°C and 25°C. During the first 24 hours, an average of 29.8% of AITC was transformed, or degraded, and over the first 10 days at 20°C, an average of 97.1% was degraded (Borek et al., 1995). Mean half-life was reported to be approximately 47 hours. The data also demonstrate that AITC transforms in sterilized soil at the same rate as intact soil, indicating that microbial populations are not responsible for the degradation (Borek et al., 1995). There was no correlation between degradation rates and pH.

However, Price et. al. (2005), in a study investigating the degradation of AITC-containing plant (*Brassica* spp.) tissue in soil, demonstrated that AITC degradation was over 3X greater in nonautoclaved soils vs. autoclaved soils, suggesting that microbial degradation is a major pathway of AITC dissipation from soil. In addition, in nonautoclaved, covered soils, degradation was relatively rapid. In unautoclaved, covered soils, AITC concentrations increased from 0.90 umol/L at 15 min post application to 1.39 umol/L at 8 hours (54% increase) then rapidly declined to 0.77 umol/L (45% decrease) at 24 hours post application. The spike in volatile AITC concentration at 4 hours post application was attributed to the trapping of AITC volatiles by the tarp covers, prior to full activation of soil degradation processes and the full depletion of AITC source material in the plant tissue.

Based on the data from Price et. al. (1997), if AITC degrades 45% in 16 hours from its highest concentration in soil (between 8 and 24 hours post application), then it is estimated that AITC is likely to degrade to nondetectable levels in soil in:

$$\frac{45\%\ \text{degradation}}{16\ \text{hours}} = \frac{100\%\ \text{degradation}}{X\ \text{hours}}$$

$$\mathbf{X = 35\ hours}$$

Based on the calculated estimate above and the data from Price et. al. (1997), AITC is likely to degrade to nondetectable levels in approximately 35 hours after reaching its peak concentration in soil (4 hours), or approximately 39 hours post application.

This is comparable to the data reported by Borek et. al. (1995; as cited in MRID 48822108) that demonstrated that AITC degraded in soil with a mean half life (for six different soils) of 47 hours. **Extrapolating these data indicates that AITC is likely to be degraded to nondetectable levels by no more than approximately 98 hours (approximately 4 days) post application.**

1. Major Degradates of AITC

Possible degradation products of AITC in soil can be proposed based on the decomposition products of AITC present in an aqueous solution in the pH range between 6 and 8, where AITC is proposed to degrade completely (Pecháček et al., 1997 as cited in MRID 48824108). Within this pH range, it was observed that the primary decomposition products identified at 80 °C and in lower quantities at 20 °C and 40 °C after an 80 min incubation, were: allyl thiocyanate (ATC); allylamine (AA); and carbon disulfide (CDS). All three degradates, as well as AITC, are expected to rapidly volatilize from the surfaces of uncovered soils and be subject to rapid degradation in the atmosphere, particularly via reaction with photochemically-produced hydroxyl radicals.

Once volatilized into the atmosphere, AITC, AA and CDS are expected to have half lives of 2.4 hours, 2.4 hours, 6.9 hours, and 5.5 days, respectively. Atmospheric degradation of ATC is expected to be similar to that of AITC based on its ready interconversion to AITC. These data indicate that if AITC or any of its degradates should escape from beneath tarped or compacted soils, it will be rapidly diffused and degraded in the atmosphere.

A. Allylthiocyanate (ATC)

ATC is an isomer of AITC and as such is expected to dissipate as rapidly as its parent, AITC. ATC is in a reversible equilibrium with AITC. Based on data from the study in aqueous solution by Pecháček et al. (1997 as cited in MRID 48824108), when AITC is incubated at pH 6.0 and 80 °C it ATC concentration increases initially from 1.0 millimoles/liter (mM/L) at time 0 to a maximum of 3.6 mM/L at 20 min incubation and declines to 1.0 mM/L at 80 min at pH 6.0, a 72% decline in 60 minutes. Based on the data above, ATC is expected to dissipate no less rapidly than AITC in moist soils and likely will not be present at detectable levels by the time the parent AITC declines to nondetectable levels (no more than approximately 47 hours post application).

B. Allylamine

Allylamine (AA) is readily biodegradable in soil and water (HSDB, 2013b). AA was degraded 89% in 4 weeks using an activated sludge inoculum at 30 mg/L in the Japanese MITI test. AA readily volatilizes into the atmosphere where it is expected to be rapidly degraded via reaction with photochemically-produced hydroxyl radicals with a half life of 6.9 hours. AA has been shown to degrade in aqueous solution at pH 6.0 and 80 °C approximately 51% in 30 minutes.

C. Carbon disulfide

Carbon disulfide (CDS) is a "natural product of anaerobic biodegradation and is released to the atmosphere from oceans and landmasses as well as geothermal sources. The ocean appears to be a major source of carbon disulfide. It is a natural constituent of the Acacia tree and the valley oak (Coastal and marshland areas of high biological activity are also a major source." (HSDB, 2013c). Although it would appear that biodegradation does not play a large role in the dissipation of CDS as it is used as a disinfectant and is toxic to bacteria, a study by Alcantara et. al. (1999) CDS was reported to be degraded 100% by gram negative bacteria in 5 to 8 hours. It can be transformed by reactions with amino acids and proteins and via reaction with the P-450 monooxygenase system (WHO, 2000); these components are likely present in microbe rich soils. In addition, CDS has been demonstrated to be degraded aerobically and anaerobically by the soil microbes *Thiobacillus thioparus* TK-m and Paracoccus denitrficans (BioCyc, 2013); it is also metabolized in the leaves of CDS producing plants, where it is produced as a natural fungicide.

CDS has a weak UV adsorption band at 317 nm, suggesting a potential for direct photolysis, although this is not a major atmospheric degradation pathway. It hydrolyzes slowly to carbon dioxide and hydrogen disulfide in alkaline solutions. It volatilizes from uncovered soil and water surfaces very rapidly and is expected to be degraded via reaction with photochemically-produced hydroxyl radicals within 5.5 days (HSDB, 2013c). Other atmospheric data indicates that oxidative processes in the atmosphere will degrade CDS with within 12 days (ASTDR, 1996). In a review by WHO (2000), a soil treatment study with 50% carbon disulfide found that concentrations of CDS declined rapidly after application and were nondetectable within 24 hours

Based on the weight of evidence, the data indicate that CDS will rapidly degrade via microbial activity in the soil if covered with tarps immediately following application or deep injected followed by soil surface compaction, and in the atmosphere.

2. Summary

AITC and its major degradates are expected to rapidly degrade in soil following application according to proposed label use instructions (tarp covered and deep injected following application). AITC and its structurally similar isomer ATC, with which it readily interconverts, are expected to completely degrade in soil in approximately 4 days post application. The remaining two degradates are expected to rapidly degrade by microbial activity in the soil in time frames that are much less than 5 days based on the weight of laboratory evidence. Should any

amount of AITC or its degradates volatilize into the atmosphere, they will be rapidly diluted and degraded via reaction with photochemically produced hydroxyl radicals

REFERENCES

Alcantara, S., I. Estrada, S. Vasquez, and S. Revah. 1999. Carbon disulfide oxidation by a microbial consortium from a trickling filter. Biotechnology Letters. 21: 815-819.

BioCyc. 2013. MetaCyc Pathway: Carbon Disulfide Oxidation (aerobic). http://biocyc.org/META/NEW-IMAGE?type=PATHWAY&object=PWY-5336 (Accessed 09/17/2013)

HSDB (Hazardous Substances Data Bank). 2013a. Allyl Isothiocyanate. Environmental Fate and exposure summary. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB (Accessed 09/17*2013)

HSDB (Hazardous Substances Data Bank). 2013b. Allylamine. Environmental Fate and exposure summary. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB (Accessed 09/17/2013)

HSDB (Hazardous Substances Data Bank). 2013c. Carbon disulfide. Environmental Fate and exposure summary. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB (Accessed 09/17/2013)

Price, J. P., C. S. Charron, A. M. Saxton, and C. E. Sams. 2005. Allyo Isothiocyanate and carbon dioxide produced dueing degradation of *Brassica juncea* tissue in different soil conditions. HortScience 40(6): 1734-1739. http://hortsci.ashspublications.org/content/40/6/1734.full.pdf

World Health Organization (WHO). 2000. Carbon Disulfide. Air Quality Guidelines, 2nd Edition. WHO Regional Office for Europe, Copenhagen, Denmark. http://www.euro.who.int/__data/assets/pdf_file/0019/123058/AQG2ndEd_5_4carbodisulfide.PDF

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August 21, 2013

RE: IR9804 (EPA File Symbol 89285-R)
Response to Agency question communicated via email dated 8/15/2013

Dear Linda and Gina:

On August 15, 2013 the following question was communicated via email:

> "Management is requesting more information on the soil degradates of AITC (allylamine, carbon disulfide, and ATC) before moving forward with these registrations. Does Isagro have quantitative information on the half-life of these compounds? And/or is there information availability to demonstrate low or no toxicity?"

In response, as noted in the original submission the primary decomposition products of AITC in aqueous solutions identified in the pH range between 6 and 8 are: 1) allyl thiocyanate (ATC), 2) allylamine (AA), and 3) carbon disulfide (CDS) (Pecháček et al., 1997). These were identified as possible degradation products of AITC in the soil following application, since the soil AITC treatments occur in the presence of water (MRID No. 488241-08).

Allyl thiocyanate (ATC)

ATC has been identified as an isomer of AITC rather than a degradation product per se as shown in Scheme 1 provided below (from Pecháček et al., 1997; MRID No. 488241-08). As shown in Tables 2 and 3 (also by Pecháček pasted below), the ATC concentration increases initially when AITC is put in aqueous solution and then declines after 50 or 60 minutes as the AITC degrades. Thus, the increase in ATC is short-lived and ATC is either further degraded or converted back to AITC as there is a change in the equilibrium of the isomers shown in Scheme 1 when AITC is lost / degraded. Ultimately ATC is expected to have a short half-life (T1/2) on the order of hours, in the

soil when applied according to label directions, particularly when soil is tarped following application.

Scheme 1. Major Path of AITC and ATC Isomerization

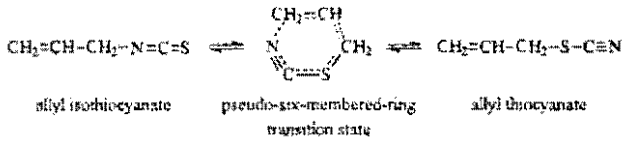

Table 2. Products Arising from AITC at pH 6[a]

	product (in mM/L)											
time (min)	AITC	ATC	DAU	DATU	ADTC	AADTC	AA	CDS	AM	DAS	DADS	total
0	10.1	1.9	nd	nd	nd	nd	nd	nd	nd	nd	nd	12.0
10	5.1	3.4	nd	nd	nd	tr	0.3	0.2	nd	0.2	tr	9.2
20	3.1	3.6	nd	nd	nd	tr	0.8	0.3	tr	0.3	tr	8.1
30	1.3	3.1	nd	nd	nd	0.1	1.7	0.7	tr	0.4	tr	7.4
40	0.7	2.7	nd	nd	nd	0.2	2.5	0.9	tr	0.4	tr	7.2
50	0.3	2.4	nd	tr	nd	0.2	2.9	1.5	0.1	0.3	tr	7.6
60	0.2	1.7	nd	tr	nd	0.2	3.1	1.7	0.1	0.2	tr	7.3
70	0.1	1.2	nd	tr	nd	0.2	2.7	1.7	0.2	0.2	tr	6.4
80	0.1	1.0	nd	tr	nd	0.2	1.4	2.0	0.3	0.2	tr	5.2

[a] tr, traces (0.01−0.04 mmol dm^{-3}); nd, not detected.

Table 3. Products Arising from AITC at pH 8[a]

	product (in mM/L)											
time (min)	AITC	ATC	DAU	DATU	ADTC	AADTC	AA	CDS	AM	DAS	DADS	total
0	10.1	2.0	nd	nd	nd	nd	nd	nd	nd	nd	nd	12.2
10	8.0	2.4	nd	tr	1.9	nd	0.5	nd	nd	nd	tr	12.8
20	5.4	3.1	tr	0.3	2.6	0.1	1.2	tr	nd	nd	tr	12.7
30	2.9	3.5	0.1	0.6	2.9	0.2	2.1	0.1	tr	0	tr	11.4
40	1.7	3.3	0.1	0.7	3.1	0.2	2.9	0.3	tr	0	tr	12.1
50	0.7	2.6	0.2	0.9	3.1	0.2	3.6	0.3	tr	0.1	tr	11.8
60	0.2	2.2	0.1	0.6	3.1	0.1	4.2	0.5	tr	0.1	tr	11.1
70	0.1	1.4	0.1	0.9	3.1	0.8	4.6	0.6	tr	0.2	tr	11.8
80	0.1	0.3	0.2	1.1	3.1	0.6	5.0	1.1	tr	0.3	0.1	11.7

[a] tr, traces (0.01−0.04 mmol dm^{-3}); nd, not detected.

Allylamine (AA)

According to the Hazardous Substance Data Base (HSDB), AA derived from application of AITC to soils is expected to volatilize into the air where it has a short half-life, or readily biodegrade (HSDB, NLM). In addition, Table 2 (Pecháček et al, 1997) indicates that AA began to degrade after reaching a peak concentration an hour after AITC entered an aqueous solution, indicating that AA further decomposes in aqueous solutions. According to the HSDB, AA is expected to volatilize from moist soil surfaces based upon an estimated Henry's Law constant of $1.82X10^{-5}$ atm-cu m/mole, and : "Allylamine is expected to volatilize from dry soil surfaces based upon its vapor pressure." Further the HSDB states: "Vapor-phase allylamine will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 6.9 hours." AA has also been shown to be readily biodegradable in the Japanese MITI test (HSDB), which suggests that AA may

biodegrade following application while the application site remains tarped. Together this information indicates that AA decomposes and / or biodegrades in the soil while covered by the tarp, and any remaining AA will volatilize from the soil to the air where it has a half-life of 6.9 hours.

Carbon disulfide (CDS)

CDS is a volatile compound that generally evaporates from soil and surface water very rapidly, but when applied to soil that is covered according to label directions, AITC is likely to be oxidized by gram-negative soil microbes. According to the Agency for Toxic Substances & Disease Registry (ATSDR), CDS has a low tendency to be retained by soils and CDS released to soils will rapidly volatilize to the atmosphere (ATSDR, 1996). The estimated half-life of CDS in the atmosphere due to oxidation is 12 days. Quoting from the ATSDR Toxicological Profile for CDS, "since the chemical is rapidly volatilized (high Henry's law constant) and probably highly mobile in soil (low Koc), it is unlikely that it remains in the soil long enough to be significantly biodegraded." That said, the proposed application methods for AITC on the label call for covering and or appropriately sealing the treated soil with tarps or mechanical means described on the proposed product label, which provides additional time for CDS biodegradation in the soil. The ATSDR Profile states that biodegradation of CDS by microbes isolated from soil has been reported. An article published after the Profile was written reports that CDS is oxidized by gram negative bacteria at a rate of 3.4 mg CDS/$g_{protein}$min at 30°C and pH 7 (Alcántara, 1999). In the study, 12mM CDS degraded completely in 5 to 8 hours. This suggests that the AITC that is degraded to CDS likely further degrades before the tarps are removed. Direct photolysis does not play a significant role in CDS breakdown in air. Any CDS that makes it to surface waters is expected to volatilize with a half-life of about 11 minutes according to ATSDR (1996). Ultimately CDS will either breakdown in the soil after application to innocuous by-products, or it will volatilize into the air where it has a half-life of about 12 days.

References

Alcántara S, Estrada I, d Vásquez S & Revah S. 1999. Carbon disulfide oxidation by a microbial consortium from a trickling filter. Biotechnology Letters 21: 815–819.

ATSDR, 1996. Toxicological Profile for Carbon Disulfide. 5.3 ENVIRONMENTAL FATE. Agency for Toxic Substances and Disease Registry; Centers for Disease Control; Atlanta, GA.

http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=474&tid=84

HSDB, NLM, 2013 viewed. Allylamine. Environmental Fate and Exposure Summary Provided in Appendix I. (section attached below)

With this response we believe we have fully addressed the question. Let me know if there are any further questions or comments.

Regards,

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APPENDIX I. Excerpt from the HSDB, Allylamine entry:

Environmental Fate & Exposure:

Environmental Fate/Exposure Summary:
Allylamine's production and use in organic synthesis, as a pharmaceutical intermediate, and as a corrosion inhibitor in steel pickling(1,2) may result in its release to the environment through various waste streams. If released to air, a vapor pressure of 242 mm Hg at 25 deg C indicates **allylamine** will exist solely as a vapor in the atmosphere. Vapor-phase **allylamine** will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 6.9 hours. Vapor-phase **allylamine** will also be degraded in the atmosphere by reaction with ozone; the half-life for this reaction in air is estimated to be 23 hours. Based on its UV spectrum, **allylamine** is not expected to be susceptible to direct photolysis by sunlight. **Allylamine** is miscible in water; therefore, some removal of atmospheric **allylamine** may occur through dissolution into clouds and wet deposition. If released to soil, **allylamine** is expected to have very high mobility based upon an estimated Koc of 24. The pKa of **allylamine** is 9.70, indicating that this compound will exist predominantly in cation form in the environment and cations generally adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts. Volatilization from moist soil surfaces is expected to occur based upon an estimated Henry's Law constant of 1.82X10-5 atm-cu m/mole. **Allylamine** is expected to volatilize from dry soil surfaces based upon its vapor pressure. Utilizing the Japanese MITI test, 89% of the theoretical BOD was reached in 4 weeks classifying **allylamine** as readily biodegradable which suggests that biodegradation is an important environmental fate process in soil and water. **Allylamine** also biodegraded in other aqueous biodegradation studies. If released into water, **allylamine** is not expected to adsorb to suspended solids and sediment based upon the estimated Koc. Volatilization from water surfaces is expected to occur based upon this compound's estimated Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 39 hours and 14 days, respectively. An estimated BCF of 3 suggests the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyze under environmental conditions. Biodegradation is expected to be an important environmental fate process in water. Occupational exposure to **allylamine** may occur through inhalation and dermal contact with this compound at workplaces where **allylamine** is produced or used. No monitoring or use data are available to indicate exposure potentials to the general population. (SRC)
PEER REVIEWED

REFERENCES

Biotechnology Letters 21: 815–819, 1999.

Carbon disulfide oxidation by a microbial consortium from a trickling filter

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Key words: carbon disulfide, hydrogen sulfide, sulfur oxidizing consortia, thiobacilli

Abstract

Biological oxidation rates of CS_2 with a mixed microbial culture obtained from a trickling filter were optimal with 3 mM CS_2, pH 7, 30 °C and SO_4^{2-} below 25 g l^{-1}. Degradation rates were 3.4 mg $CS_2/g_{protein}$min and 13.8 mg $H_2S/g_{protein}$min. The concentrations of intermediates (H_2S, COS and S^0) and the product (SO_4^{2-}) of CS_2 oxidation were measured. The biological oxidation was due principally to Gram negative bacteria.

Introduction

High amounts of exhaust air contaminated with H_2S and CS_2 are generated in the traditional process for the production of cellophane and rayon. The gases are produced when the dissolved sodium cellulose xanthogenate (viscose) is precipitated in an acid bath. Concentrations for each gas in the air can be as high as 2 g m^{-3} (Acosta *et al.* 1999).

CS_2 has been classified in the US as a hazardous air pollutant in Title III of the Clean Air Act Amendments (CAAA) of 1990. H_2S is subject to a stringent control for its environmental release due to its toxicity, unpleasant odor and corrosive properties (Janssen *et al.* 1997).

There are microbial species that use reduced sulfur compounds as energy source for their growth. The sulfoxidizing capacity is utilized in different biotechnological process for the elimination of these compounds from gas and water streams. These include the use of photosynthetic, chemoautotrophic and heterotrophic bacteria and even molds. A mixed chemical biological system using chemical precipitation and microbial oxidation was used by Asai *et al.* (1990). Cork & Ma (1982) have proposed the use of the anaerobic photosynthetic bacterium *Chlorobium thiosulfatum* that converts the sulfide to elemental sulfur. *Thiobacillus denitrificans* has been used to greatly reduce H_2S under anaerobic conditions using nitrate as electron acceptor and O_2 under aerobic conditions (Ongchart *et al.* 1991, Sublette 1987). Cadenhead & Sublette (1990) studied other thiobacilli showing that they were able to grow on H_2S but did not offer a clear advantage over *Thiobacillus denitrificans*. Kanagawa & Mikami (1989) reported that *Thiobacillus thioparus*, in a mixed culture with heterotrophic bacteria, were able to purify air contaminated with H_2S, dimethyl sulfide $(CH_3)_2S$, methyl mercaptan (CH_3SH), and dimethyl disulfide $[(CH_3)_2S_2]$.

For the case of water treatment with high sulfide loading, Buisman *et al.* (1989) reported the direct transformation of H_2S to sulfur and sulfate by microbial oxidation. The microbial population was a mixed culture previously enriched from mud. This work led to the development of a gas treatment process through the use of a scrubber coupled to the water treatment plant.

While the literature is very extensive for H_2S biotransformation, less work has been developed for CS_2 elimination. Smith & Kelly (1988) reported that only one strain of *Thiobacillus thioparus*, among eight different thiobacilli strains studied, was able to use CS_2. This strain formed carbonyl sulfide (COS) as an inter-

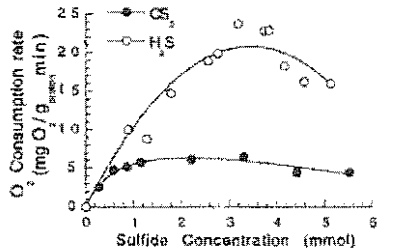


Fig. 1. Oxygen consumption rates relative to sulfide concentration of H_2S and CS_2 at 30 °C and pH 7

mediate. More recently, an unidentified *Thiobacillus* sp. (Plas *et al.* 1993) was also found to utilize CS_2 at slow growth rates. In contrast, mixed cultures showed higher sulfide oxidation rates for this compound (Plas *et al.* 1992). Torres *et al.* (1995) reported a process for the CS_2 and H_2S elimination from air streams emitted from processing viscose plants with high removal efficiencies. This system was also used to treat air emitted from a sponge plant that had only high CS_2 concentration (Acosta *et al.* 1999). The process consists of a modified trickling filter reactor where a sulfide oxidizing biofilm develops. Elimination occurs after the sulfides are absorbed in the liquid and transferred to the biofilm (Lobo *et al.* 1999). The biofilm has been shown to be very stable and to have a very complex structure consisting of bacteria, yeast, molds and higher eucaryotic (Hugler *et al.* 1996).

To improve the performance of the sulfide oxidation reactors a better understanding of the biofilm activity is required. This study reports the kinetics of a biofilm from a trickling filter degrading high CS_2 concentration in air.

Materials and methods

Organisms

The sulfoxidizing consortium was obtained from a pilot plant trickling filter adapted for the elimination of CS_2 in air waste gas containing 1.5 ± 0.3 g CS_2 m^{-3}. The reactor had been operated for more than a year when biofilm samples were withdrawn. The pH of the reactor was controlled at pH 6.0 ± 0.5. The transfer and reaction characteristics of this reactor have been described recently by Lobo *et al.* (1999).

Media and culture conditions

The consortium was grown aerobically at 30 °C in the culture medium reported by Sublette (1987). The pH was adjusted to 7.0. CS_2 was generally used as sole energy source in concentrations of 100 mg l^{-1}. For the evaluation of alternate sulfur sources, the same medium was used and supplemented with 1 mM of each sulfur species (H_2S, SO_3^{2-}, S^o and $S_2O_3^{2-}$). Closed systems using Mininert valves for growth studies were employed. Studies on the consortium were made using growth inhibitors: nystatin (8 μg ml^{-1}) and chloramphenicol (1.25 U ml^{-1}) for fungi and bacteria, respectively. Activity was determined by respirometry.

Respiration studies

To evaluate the activity of the mixed population, the method proposed by Buisman *et al.* (1989) was adapted by using free cells. The method is based on the measurement of the dissolved O_2 uptake rate and was corrected for endogenous respiration. It is reported as Mg O_2/$g_{protein}$min.

Analyses

Gaseous sulfides were analyzed by gas chromatography with a flame photometric detector. A Teflon column (1 m × 3 mm) filled with Super Q was used. The injection volume was 400 μl. The column temperature was 130 °C while the injection and detector were maintained at 150 °C and 220 °C, respectively. Sulfate, thiosulfate and sulfite were analyzed by HPLC using a photodiode array detector. A Chrompack IonoSpher A (200 × 3 mm) column was used. Potassium hydrogen phthalate (0.04 mM, pH 4.0) was used as an eluent at 0.8 ml min^{-1}. The injection volume was 20 μl. Sulfur was measured by colorimetry according to Bartlett & Skoog (1954) and protein with the Lowry method.

Results and discussion

Relative oxidation rates of sulfides and sulfur compounds

Respirometric tests were performed on samples of the biofilm formed in the trickling filter to evaluate the H_2S and CS_2 oxidation rates at different concentrations as shown in Figure 1. The same technique was

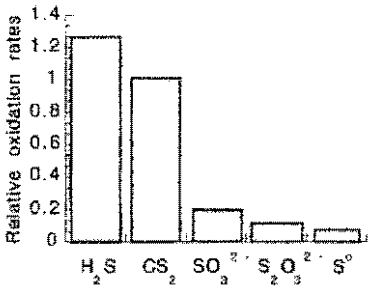


Fig. 2. Relative oxygen consumption rates of 1.0 mM H_2S, SO_3^{2-}, S° and $S_2O_3^{2-}$ (CS_2 = 1.0) at 30°C and pH 7.

Table 1. CS_2 consumption and H_2S, COS, S° and SO_4^{2-} production by the sulfoxidizing consortium at 30°C and pH 7. Initial concentrations were CS_2 0.12 mM and biomass 20 $\mu g_{protein}$ ml^{-1}.

Time (h)	Consumed CS_2 (mM)	H_2S (mM)	COS (mM)	S° (mM)	SO_4^{2-} (mM)
0	0	0	0	0	0
1	0.016	0.006	0.001	0.0004	0.03
2	0.053	0.041	0.002	0.0007	0.10
3	0.082	0.035	0.007	0.0011	0.14
4	0.107	0.024	0.004	0.0013	0.19
5	0.117	0.002	0.042	0.0015	0.20
8	0.119	0	0	0.0015	0.21
9	0.119	0	0	0.0015	0.21

used to evaluate the relative rates for different reduced sulfur species, (H_2S, CS_2, SO_3^{2-}, S°, $S_2O_3^{2-}$), at 1 mM, as depicted in Figure 2.

The higher H_2S oxidation rates observed could be explained by the fact that this compound is produced as an intermediate in the CS_2 oxidation. Furthermore, H_2S oxidation has been reported to be preferred over CS_2 by the sulfide oxidizing bacteria (Smith & Kelly 1988, Plas *et al.* 1993).

By adjusting a saturation model to the data and using the stoichiometry of sulfide oxidation, maximum degradation rates of 3.4 mg $CS_2/g_{protein}$min and 13.8 mg $H_2S/g_{protein}$min were achieved at optimal pH and temperature conditions. The saturation rates (Ks) for CS_2 and H_2S were 0.19 mM and 1.3 mM, respectively. The rate values are comparable to those reported for thiobacilli in pure culture: 4.3 mg $CS_2/g_{protein}$min, Ks 0.013 mM CS_2 (Smith & Kelly 1988); 2.5 mg $CS_2/g_{protein}$min (Plas *et al.* 1993); 5.4 mg $CS_2/g_{protein}$min, Ks 0.033 mM CS_2 (Jordan *et al.* 1995). Very low inhibition was observed for both H_2S and CS_2 at the range studied. Plas *et al.* (1993) reported total microbial inhibition at a CS_2 concentration higher than 2 mM.

As may be observed in Figure 2, elemental sulfur oxidation rate was the lowest as compared to the other sulfur species. From rate experiments data (not shown), similar to those in Figure 1, maximum rate and Ks values were 0.06 mg $S^\circ/g_{protein}$min and 4.2 mM S°. Similar results have been found with pure strains (Jordan *et al.* 1995). Low rates have been attributed to the S° solubility. Thiosulfate and sulfite were also oxidized by the consortia at rates about five times slower than CS_2 at 1.0 mM.

Oxidation intermediates of CS_2

Smith & Kelly (1988) suggested that CS_2 was transformed by *Thiobacillus thioparus* through the following reactions:

Carbondisulfide	$CS_2 + H_2O$	$\rightarrow COS + H_2S$
	$COS + H_2O$	$\rightarrow CO_2 + H_2S$
Hydrogensulfide	$2H_2S + O_2$	$\rightarrow 2S^\circ + H_2O$
Sulfur	$2S^\circ + 2H_2O + 3O_2$	$\rightarrow 2H_2SO_4$

Elemental sulfur production from CS_2 has only been reported with pure strains (Jordan *et al.* 1995), but it is very common from H_2S under O_2 controlled conditions (Janssen *et al.* 1997). To determine the intermediates formed in the CS_2 oxidation, a kinetic study and the sulfur balance were performed. As seen in Table 1, H_2S, COS, S° and SO_4^{2-} were detected from the first hour of cultivation. H_2S accumulated from CS_2 as it was being consumed. H_2S was detected at these low concentrations as its uptake rate was slower than that for CS_2 as indicated by the Ks value. COS was detected at very low concentrations and sulfur accumulated. Ninety-five percent of the initial sulfur was found as products after 9 h. The rest was possibly transformed into biomass and other intermediates.

Effect of pH on the oxidation rate

Optimum pH range was between 6 and 7 which corresponded to the pH set to control the reactor. The oxidation rate was more affected by alkaline conditions. At pH 8.0, the rate was reduced by approximately 70% while at pH 6.0 and pH 5.0 reductions

Table 2. Microbial growth and sulfide oxidation activity for the sulfoxidizing consortia on culture media amended with growth inhibitors. CS_2 (100 mg l^{-1}) was used as substrate at 30 °C and pH 7.

Microorganism media	Molds	Yeast	Bacteria	CS_2 oxidation activity mg $CS_2/g_{protein}$ min
Sabouraud+ Chloramphenicol (1.25 U ml^{-1})	(+ + +)	(+ + +)	(−)	0.3
Mineral media + Nystatin (8 μg ml^{-1})	(−)	(−)	(+ + +) Gram-negative	2.8

were around 20% and 45%, respectively. At pH 9.5 and higher, oxidation was very slow and abiotic. It is known that growth as a function of pH depends on the *Thiobacillus* species (Robertson & Kuenen 1991). Buisman *et al.* (1989) reported a consortium of sulfur colorless bacteria that shown maximum activities at the pH range 8.0–8.5, while Sublette (1987) reported a pH 7.0 for growth at pure culture of *Thiobacillus denitrificans*.

Effect of temperature on the oxidation rate

Optimum temperature for CS_2 oxidation was 30 °C. The oxidation was reduced by 85% at 20 °C and by 95% above 40 °C. Similar optimum temperatures ranges have been reported in the literature. Buisman *et al.* (1989) reported optimal temperature for a sulfoxidizing consortium in the range 25–35 °C while Sublette (1987), found that *Thiobacillus denitrificans* growth on thiosulfate was optimal at 30 °C. Lobo *et al.* (1999) reported that temperature has an important effect on the overall process as it affects solubility and transport of the gas. According to Robertson & Kuenen (1991) the majority of the well-studied species of colorless sulfur bacteria are mesophiles.

Effect of sulfate on oxidation rate

It is well documented that SO_4^{2-}, the final oxidation product, exerts a negative effect on sulfide oxidation probably due to ionic strength effects (Ongcharit *et al.* 1991). Respirometric assays showed a reduction in the CS_2 oxidation rate at increasing sulfate concentration. Fifty percent of the sulfoxidizing activity was lost as the sulfate concentration increased to 25 $g\,l^{-1}$. Smaller decrements were found at higher sulfate levels (Figure 3). In a compost biofilter system, Yang & Allen (1994) reported that 25 mg S (as SO_4^{2-})/g (dry compost basis) and lower did not show effect on H_2S oxidation. However, they observed significant inhibiting effect at higher sulfate contents. These authors suggest that a sulfate content of 25 mg S g^{-1} is a critical level for the microbial environment. Ongcharit *et al.* (1991) reported that a sulfate concentration of 20–25 g l^{-1} inhibited sulfide oxidation by *Thiobacillus denitrificans*.

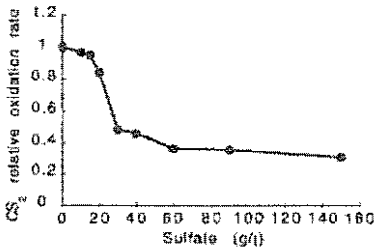


Fig. 3. Effect of sulfate concentration on CS_2 oxidation rate by the sulfoxidizing consortium at 30 °C and pH 7.

Effect of growth inhibitors on the sulfoxidizing activity of the consortium

It was demonstrated, (Hugler *et al.* 1996), that an heterogeneous microbial community (fungi, yeast and bacteria), develops on the support of the trickling filter reactor and performs the sulfide oxidation. To evaluate the relevance of the molds and yeast on the sulfide elimination, culture media were amended with growth inhibitors for bacteria or fungi. The results are depicted on Table 2.

Sabouraud medium plus chloramphenicol supported good fungi and yeast growth but little CS_2 oxidizing activity was found (0.3 mg $CS_2/g_{prot.}$ min). These microorganisms have, nevertheless, an important role in film formation (Hugler *et al.* 1996).

Mineral medium plus nystatin supported good bacterial growth while fungi and yeast were inhibited. The bacteria were Gram-negative, small cocci (0.5–1 μm), singly, in pairs or in chains. These observations indicated that these bacteria probably belong to the thiobacilli species. According to CS_2 oxidation rates, the bacteria from the consortium were mainly responsible for the CS_2 elimination (2 mg CS_2/g$_{protein}$/min).

While in biotrickling filters the transfer and equilibrium aspects of the reactor play a very important role (Lobo *et al.* 1999) the analysis of the local microbial kinetics, as shown in this paper, allows to select the relevant set points to override reaction limitations.

References

Acosta C, Walter H, Benavente JL, Revah S (1999) Biologial removal of carbon disulfide from waste air streams. *Environ. Progress* (accepted).

Asai S, Konishi Y, Yabu T (1990) Kinetics of absorption of hydrogen sulfide into aqueous ferric sulfate solutions. *AIChe J.* 36: 1331–1338.

Bartlett J, Skoog D (1954) Colorimetric determination of elemental sulfur in hydrocarbons. *Anal. Chem.* 26: 1008–1011.

Buisman C, Post R, Ijspeert P, Geraats G, Lettinga G (1989) Biotechnological process for sulphide removal with sulphur reclamation. *Acta Biotechnol.* 9: 255–267.

Cadenhead P, Sublette K (1990) Oxidation of hydrogen sulfide by thiobacilli. *Biotechnol. Bioeng.* 35: 1150–1154.

Cork D, Ma S (1982) Acid-gas bioconversion flavors sulfur production. *Biotechnol. Bioeng. Symp.* 12: 285–290.

Hugler W, Cantu-De la Garza J, Villa-Garcia M (1996) Biofilm analysis from an odor-removing trickling filter. In: *Proceedings of the Air & Waste Management Association's Annual Meeting & Exhibition*. Paper 96-WP87A.04.

Janssen A, Ma S, Lens P, Lettinga G (1997) Performance of a sulfide-oxidizing expanded-bed reactor supplied with dissolved oxygen. *Biotechnol. Bioeng.* 53: 32–40.

Jordan S, Kraczkiewicz-Dowjat A, Kelly D, Wood A (1995) Novel eubacteria able to growth on carbon disulfide. *Arch. Microbiol.* 163: 131–137.

Kanagawa T, Mikami E (1989) Removal of methanethiol, dimethyl sulfide and hydrogen sulfide from contaminated air by *Thiobacillus thioparus* TK-m. *Appl. Environ. Microbiol.* 55: 555–558.

Lobo R, Revah S, Viveros G (1999) An analysis of a trickle bed bioreactor: Carbon disulfide removal. *Biotechnol. Bioeng.* 63: 93–109.

Ongcharit C, Sublette K, Shah Y (1991) Oxidation of hydrogen sulfide by flocculated *Thiobacillus denitrificans* in a continuous culture. *Biotechnol. Bioeng.* 37: 497–504.

Pias C, Harant H, Danner H, Jelinek E, Wimmer K, Hohlbar P, Braun R (1992) Ratio of biological and chemical oxidation during the aerobic elimination of sulphide by colorless sulphur bacteria. *Appl. Microbiol. Biotechnol.* 36: 817–822.

Pias C, Wimmer K, Hohlbar P, Mallinkovich D, Danner H, Jelinek E, Harant H, Braun R (1993) Degradation of carbon disulphide by a *Thiobacillus* isolate. *Appl. Microbiol. Biotechnol.* 38: 820–823.

Robertson L, Kuenen J (1991) The colorless sulfur bacteria. In: Balow A, Trüper H, Dworkin M, Harder W, Schleifer K, eds *The Prokaryotes*, Vol. 1, 2nd ed. New York: Springer-Verlag, pp. 385–413.

Smith N, Kelly D (1988) Oxidation of carbon disulphide as the sole source of energy for the autotrophic growth of *Thiobacillus thioparus* strain TK-m. *J. Gen. Microbiol.* 134: 3041–3048.

Sublette K (1987) Oxidation of hydrogen sulfide by *Thiobacillus denitrificans*: desulfurization of natural gas. *Biotechnol. Bioeng.* 29: 249–257.

Torres C, Revah S, Hinojosa A, Paez F, Morales V (1993) Biological process for the elimination of sulfur compounds present in gas mixture. US Patent 5,236,677.

Yang Y, Allen E (1994) Biofiltration control of hydrogen sulfide 1. Design and operational parameters. *J. Air Waste Manage. Assoc.* 44: 863–868.

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Releases of carbon disulfide to the environment as a result of industrial activity are expected to be primarily to the atmosphere. Any carbon disulfide released to surface waters in effluent streams is expected to partition rapidly to the atmosphere as a result of the high ratio of vapor pressure to the solubility (Henry's law constant = 1.01×10^{-2} atm • m^3/mol) of the compound. Hydrolysis is not a significant removal mechanism since the evaporation half-life from a saturated solution is estimated to be 11 minutes (EPA 1978a).

Although no information was found evaluating the partitioning of carbon disulfide from water onto sediments, it is not expected to be removed significantly from the aquatic phase through adsorption. The low K_{oc} value, calculated from water solubility data, is 54 (EPA 1986b), indicates high soil mobility, but it probably will be less mobile in soils of high organic content.

Although Roy and Griffin (1985) did not conduct adsorption studies, they classified carbon disulfide as a mobile solvent exhibiting a low tendency to be retained by soils. Carbon disulfide released to soils in spills should rapidly volatilize to the atmosphere, but a portion of the compound remaining on soil surfaces could be available for transport into groundwater since it does not have much affinity for soil particles. Farwell et al. (1979) indicated that carbon disulfide volatilizes from a variety of soils, although rates were not provided.

No experimental data on biomagnification were found in the available literature. Estimated bioconcentration factor (BCF) values (equal to 2.94×10^3) were calculated from solubility and K_{ow}, (log K_{ow} is 2.16) data. The calculated values, 6.8 and 25.8 respectively for solubility and K_{ow} data, indicate that carbon disulfide will not significantly bioaccumulate in aquatic organisms (EPA 1986b).

5.3.2 Transformation and Degradation

5.3.2.1 Air

Carbon disulfide reacts with hydroxyl radicals in the troposphere to produce carbonyl sulfide (Cox and Sheppard 1980). The lifetime of carbon disulfide in the troposphere, assuming a reaction rate constant of 4.3×10^{-13} cm^3 $molecule^{-3}$, is =73 days (uncertain); other estimates (assuming different reaction rate constants) range from less than 1 week to more than 10 weeks (Cox and Sheppard 1980; EPA 1978a; Wine et al. 1981).

The photo-oxidation products of carbon disulfide in the laboratory were identified as carbon monoxide, carbonyl sulfide, sulfur dioxide, and a polymer that adhered to the sides of the reaction vessel (Heicklen et al. 1971). Although carbon disulfide absorbs light at wavelengths between 280 and 350 nm, dissociation does not occur under environmental conditions because of low molar absorptivity (Atkinson et al. 1978; Wood and Heicklen 1971) and direct photolysis of carbon disulfide in the atmosphere does not appear to be significant. EPA (1978a) stated that the information available indicated that carbon disulfide is relatively persistent in the atmosphere. For the atmospheric oxidation of carbon disulfide to sulfur dioxide, car-bonyl sulfide, and carbon monoxide, the half-life was estimated to be about 12 days.

According to Wine et al. (1981), electronically excited carbon disulfide is rapidly produced in the troposphere from absorption of solar photons. This excited carbon disulfide reacts with oxygen on a time scale of 1-2 weeks to yield car-bonyl sulfide, the predominant sulfur-containing compound in the troposphere.

The lifetime of carbon disulfide in the atmosphere has been estimated to be 12 days, too short a time to reach the stratosphere. Removal was suggested to occur by a hydroxyl radical reaction, or an oxygen atom reaction but not by dissociation (Khalil and Rasmussen 1984).

Based on the estimates of a lifetime in the troposphere for carbon disulfide on the order of weeks and the troposphere to stratosphere turnover time on the order of years, very little tropospheric carbon disulfide is expected to be transported to the stratosphere (EPA 1986b).

5.3.2.2 Water

Carbon disulfide is stable to hydrolysis in the pH region of environmental concern (pH 4-10). At pH 13, carbon disulfide has a hydrolysis half-life at of about 1 hour at 25°C; by extrapolation, at pH 9, carbon disulfide has a half-life of 1.1 years (EPA 1978a). In oxygenated seawater, carbon disulfide was found to be stable for over 10 days (Lovelock 1974). The volatilization half-life from a saturated water solution has been estimated to be 11 minutes (EPA 1978a). The compound apparently does not undergo biodegradation at rates that are competitive with its volatilization from surface waters.

5.3.2.3 Sediment and Soil

No data were found in the available literature on the biodegradation of carbon disulfide in soil. However, since the chemical is rapidly volatilized (high Henry's law constant) and probably highly mobile in soil (low K_{oc}), it is unlikely that it remains in the soil long enough to be significantly biodegraded.

Microbial degradation of large amounts of carbon disulfide in soil would not be expected to be significant since this compound is a soil disinfectant and toxic to bacteria. Hydrolysis of carbon disulfide on wet soil surfaces is also unlikely (EPA 1986b). Oxidation of carbon disulfide by a Thiobacillus species isolated from soil has been observed (Pfas et al. 1993).

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

Carbon disulfide was detected at 41 parts per trillion (ppt) in 61 rural samples and at 65 ppt in 88 urban/suburban air samples collected by Brodzinsky and Singh (1983). Carroll (1985) sampled air in the vicinity of San Juan, Puerto Rico; Albany, New York; and Wallops Island, Virginia. Carbon disulfide showed considerable spatial variability and a correlation with cloud activity. It was observed that the ocean appears to be a source of carbon disulfide. The air at Wallops Island coming in from the ocean had levels of 30 ppt. Air samples taken at Sapelo Island, Georgia, revealed carbon disulfide levels of about 380 ppt above a saltwater marsh, about 100 ppt above a freshwater marsh, and

Pages 57-72 are a publicly available science review located in Regulations.gov at:

http://www.regulations.gov/index.jsp#!documentDetail;D=EPA-HQ-OPP-2013-0658-0005

BPPD New Product/Non-Registered AI Source Readiness Screen

Date: 10/18/2012

Review Date: 10/18/2012

File Symbol No.: 89285-R

Reviewers: Colin Walsh & Sadaf Shaukat

BPB/MPB: BPB

Comments: Note to Reviewer: The a.i., AITC, has a proposed use pattern of a pre-plant soil treatment (fumigant).

Pass/Fail: PASS

Hours Worked: 1.0 hour

	Checklist Item	Yes	No	N/A	Comments
1.	**Forms**				
a.	8570-1: Application for Registration	X			
b.	8570-4: CSF	X			
c.	8570-27: Formulator's Exemption			X	
d.	8570-34: Certification with Respect to Data	X			
e.	8570-35: Data Matrix	X			
2.	**Confidential Statement of Formula (CSF)-review for alternate formulations too**				
a.	Signed and dated	X			
b.	Food-use? (If no, skip to 1e.)		X		
c.	All inerts cleared for food-use				
d.	Active cleared for food-use				
e.	All inerts cleared for nonfood-use (skip if food-use)			X	Only a.i. and impurities
f.	Conventional or antimicrobial actives present?		X		
g.	CSF accurately reflects label	X			
h.	Active(s) + Inert(s) = 100%	X			
i.	CAS #s for all inerts			X	
j.	Chemical names provided for inerts			X	
k.	Units in all applicable boxes	X			

l.	Proprietary inerts? If so, is info. on file with the Agency?			X	
m.	Supplier information adequately listed	X			
n.	Certified limits correct?	X			
o.	If certified limits are outside recommended range, explanation provided?			X	
p.	Microbial: culture collection reference			X	
q.	Microbial: strain designation for a.i.			X	
r.	Microbial: potency provided with a.i.			X	
s.	Alternate formulations?		X		
t.	Are alternate formulations actually alternate and not a new product?			X	
3.	**Data Matrix-ACTIVE INGREDIENT**				
a.	Separate data matrix for the source of AI			X	See Data Matrix for MP below (section 4)
b.	All product chemistry data requirements addressed (guideline by guideline)				
c.	All toxicology data requirements addressed (guideline by guideline)				
d.	All nontarget toxicology data requirements addressed (guideline by guideline)				
e.	Reflects info. reported on CSF (e.g.: identity of AI)				
Note for 3b.-d. above: if not addressed in data matrix, may be addressed in elsewhere in submission					
4.	**Data Matrix-MP or EP**				
a.	Separate data matrix for the product	X			
b.	All product chemistry/product analysis data requirements addressed (guideline by guideline)	X			
c.	All mammalian/human health toxicology/ pathogenicity data requirements addressed (guideline by guideline)	X			

d.	All Tier 1 nontarget organism toxicology/ pathogenicity data requirements addressed (guideline by guideline)	X			
e.	Efficacy data (if public health pests on label)			X	
f.	HSRB review required?		X		
5.	**Data Requirements-Guideline Studies**				
Note: This section is for submitted guideline studies only. See below for waivers and rationales.					
a.	Product chemistry: do all submitted studies appear to satisfy the data requirements?	X			
b.	Toxicology: do all submitted studies appear to satisfy the data requirements?	X			The applicant indicated on the data matrix that the primary eye irritation study is in MRID 488241-08; however, the study is not addressed in the MRID. The applicant addressed this data requirement in the application materials under cover letter dated August 29, 2012 (page 2 of 3).
c.	Nontargets: do all the submitted studies appear to satisfy the data requirements?			X	
d.	Other (residue data, special studies, etc.)			X	
6.	**Data Requirements- Waivers**				
Note: This section is for waivers only. This does not apply to rationale submitted to satisfy the data requirements.					
a.	Are there any requests for waivers? Please note.			X	See Rationales/Literature (section 7) below.
b.	For each applicable data requirement, does the waiver request have a separate scientific rationale justifying why testing is not applicable?				
c.	Does each waiver request seem reasonable and justified?				
7.	**Data Requirements- Rationales/Literature**				
Note: This section is for rationales only. This does not apply to requests submitted to waive the data requirements.					
a.	Have rationales been submitted in lieu of guideline studies? Please note.	X			Data waiver rationales have been submitted for the toxicity (excluding acute toxicity) and nontarget organisms.
b..	Does each rationale have scientific literature citations where applicable?	X			

c.	Are the rationale and scientific citations organized in reasonable order to facilitate timely review and is each guideline addressed individually?	X			
d.	Are copies of cited scientific literature included in the package?	X			
e.	Does the rationale appear to be reasonable and scientific?	X			
8.	**Label**				
a.	Restricted Use Pesticide statement (If applicable)			X	
b.	Product name, brand or trademark	X			
c.	Ingredient statement correct? Microbial: strain designation Microbial: potency designation	X			
d.	"Keep Out of Reach of Children" (KOOROC) Statement	X			
e.	Signal word	X			
f.	First aid statement	X			
g.	Net contents/net weight	X			
h.	EPA Reg. No. and Establishment No.	X			
i.	Company name and address	X			
j.	Precautionary statement: hazards to human and domestic animals Microbial: dusk mask statement	X			
k.	Environmental hazards	X			
l.	Physical and chemical hazards (if app.)			X	The CSF indicates a flammability of 47°C. The EP is considered combustible and must have the appropriate language.
m.	Directions for use	X			
m.	Storage and disposal	X			
o.	Warranty statement	X			
p.	Worker protection			X	
q.	Batch code		X		Batch code is required

PRIA 2 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

3/23/09

21 Day Screen Start Date: 8/31/12

Experts In-Processing Signature: MP Date 9/5/12 Fee Paid: Yes ✓

Division management contacted on issues No_____ Yes _____ Date _____

EPA Reg. Number: 89285-R	EPA Receipt Date: 8/31/12

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1)(link to form) signed & complete including package type			X		
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4) (Link to form)			X		
	a) All inerts (link to http://www.epa.gov/opprd001/inerts/), including fragrances, approved for the proposed uses (see Footnote A) No inerts	yes	no			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) (Link to form) completed and signed (N/A if 100% repack)			X		
	Certificate and data matrix consistent			X		
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	yes	no			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) (Link to form) completed and signed (N/A if source is unregistered or applicant owns the technical)					X
5	**Data Matrix** (EPA Form 8570-35) (Link to form) both internal and external copies (PR 98-5) (Link to PR 98-5) completed and signed (N/A if 100% repack)			X		
		yes	no			
	a) Selective Method (Fee category experts use)	X				
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label (link to http://www.epa.gov/oppfead1/labeling/lrm/) (Electronic labels on CD are encouraged and guidance is available)(link to** http://www.epa.gov/pesticides/regulating/registering/submissions/index.htm#labels)			X		

7	**Is the data package consistent with PR Notice 86-5** (link to PRN 86-5)	X		
8	**Notice of Filing (link to http://www.epa.gov/pesticides/regulating/tolerance_petitions.htm) included with petitions (link to http://www.epa.gov/pesticides/regulating/tolerances.htm)**			X
9	**If applicable for conventional applications, reduced risk rationale (link to http://www.epa.gov/opprd001/workplan/reducedrisk.html)**			X
10	**Required Data (link to http://www.epa.gov/pesticides/regulating/data_requirements.htm) and/or data waivers. See Footnote C.**	X		
	a) List study (or studies) not included with application			

Comments:

COMPANY CONTACTED TO CLARIFY TITLE DISCREPANCY ON TRANSMITTAL. ISSUE WAS RESOLVED. AA 9/14/12

MRID 488241 – DATA PASSED I&S REVIEW. AA 9/14/12

TECHNICAL & IMPURITIES ONLY - NO INERTS TO REVIEW. AA 9/6/12

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses. If an unapproved inert is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. <u>All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.</u>

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses **even if a product is currently registered** by consulting the inert Web

site [link to http://www.epa.gov/opprd001/inerts/lists.html] and if the inert is not approved, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch [Link to http://www.epa.gov/oppbppd1/biopesticides/contacts_bppd.htm].

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information [link to http://www.epa.gov/opprd001/inerts/tips.pdf] must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R311, R312 or R313), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

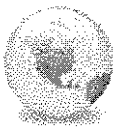
2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.



RE: Regarding Application 89285-R (IR9804)
Amy Roberts
to:
Anthony Ashe
09/13/2012 02:24 PM
Hide Details
From: Amy Roberts <ARoberts@TSGUSA.COM>

To: Anthony Ashe/DC/USEPA/US@EPA

Dear Anthony:

Sorry for that discrepancy, but those are the same data volumes and the submitted study is the intended study. I can submit an updated transmittal document if you need it, but it is the same.

Regards,

Amy Plato Roberts
Senior Regulatory Consultant
Technology Sciences Group, Inc.
712 Fifth Street, Suite A
Davis, CA 95618 USA
Phone: (530) 757-1432
Fax (530) 757-1299
www.tsgusa.com

From: Anthony Ashe [mailto:Ashe.Anthony@epamail.epa.gov]
Sent: Thursday, September 13, 2012 12:08 PM
To: Amy Roberts
Subject: Regarding Application 89285-R (IR9804)

Ms. Roberts,

This message is being sent as a follow up to a voicemail left for you regarding the above-mentioned application. There is a bit of a discrepancy between the study title of your third volume ("Analysis...") and what is listed on the

B 672

A B672 is described as a new product; non-food use or food use having established tolerance or tolerance exemption; unregistered source of active ingredient; no data compensation issues; all Tier I data requirements for product chemistry, toxicology, non-target organisms, and product performance must be addressed with product-specific data or with request for data waivers supported by scientific rationales.

This PRIA code is interpreted as an application for registration of a microbial or biochemical pesticide product that is **not** substantially similar or identical in its uses and/or formulation to products that are currently registered. These applications require product specific chemistry data, acute toxicity data and other Tier I mammalian and non-target toxicity data as determined by the general use patterns for the product. When public health pests are claimed, efficacy (product performance) data for the product must be submitted.

End Use (EP) Data. Manufacturing Use (MP) product or Technical Grade of the Active Ingredient (TGAI). This is for products with an unregistered source of active ingredient(s). These products are not 100% identical (repack)

Guideline No.	Product Chemistry Data Study Title	EP Data Submitted/ Cited		MP or TGAI Data Submitted/ Cited	
		Yes	No	Yes	No
880.1100	Product Identity & Composition	X			
880.1200	Description of starting materials production and formulation process.	X			
880.1400	Discussion on the formation of impurities	X			
830.1700	Preliminary analysis	X			
830.1750	Certified limits (158.345)	X			
830.1800	Enforcement analytical method	X			
830.6302	Color	X			
830.6303	Physical State	X			
830.6304	Odor	X			
830.6313	Stability to normal and elevated temperatures metal and metal ions				
830.6315	Flammability	X			
830.6317	Storage stability	X			
830.6319	Miscibility	X			
830.6320	Corrosion Characteristics	X			
830.7000	pH	X			
830.7050	UV/ Visible Absorption				
830.7100	Viscosity	X			
830.7200	Melting Point				
830.7220	Boiling Point				
830.7300	Density	X			
830.7550 830.7560	Partition Coefficient				

870.3250	90-day dermal - rat	X					
870.3465	90-day inhalation - rat						
870.3700	Prenatal Developmental – rat preferably						
870.5100	Bacterial Reverse Mutation Test						
870.5300 870.5375	*In vitro* mammalian cell assay	✓					

Manufacturing Use Product (MP) or Technical Grade Active Ingredient (TGAI) Non-target Organism Toxicity. The test substance must be the TGAI or MP

Guideline No.	Non-Target Organism Acute Toxicity Study Title	Data submitted		Cited		Waiver Request Rationale	
		Yes	No	Yes	No	Yes	No
850.2100	Avian Acute Oral Toxicity	X					
850.2200	Avian Dietary Toxicity						
850.1075	Fish Acute Toxicity, Freshwater						
850.1010	Aquatic Invertebrate Acute Toxicity, Freshwater						
850.4100	Terrestrial Plant Toxicity, Seedling Emergence						
850. 4150	Terrestrial Plant Toxicity, Vegetative Vigor	✓					

Efficacy – Whether or not these data are submitted depends on the proposed label use (public health pests). Data are conducted on the end-use product.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

September 5, 2012

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

OPP Decision Number: D-469288
EPA File Symbol or Registration Number: 89285-R
Product Name: IR9804
EPA Receipt Date: 31-Aug-2012
EPA Company Number: 89285
Company Name: ISAGRO USA, INC

MELVIN GRABEN
ISAGRO USA, INC
430 DAVIS DRIVE, SUITE 240
MORRISVILLE, NC 27560-

SUBJECT: Receipt of Registration Application Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your application and certification of payment. If you submitted data with this application, the results of the PRN-2011-3 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: B672

UNREGISTERED SOURCE OF ACTIVE INGREDIENT;NEW PRODUCT;Reduced Fee: Linked to PRIA Application;TIER I DATA REQUIREMENTS FOR PRODUCT CHEMISTRY, TOXICOLOGY, NON-TARGET ORGANISMS & PRODUCT PERFORMANCE MUST BE ADDRESSED WITH PRODUCT-SPECIFIC DATA OR REQUESTS FOR DATA WAIVERS WITH SUPPORTING SCIENCE;NO DATA COMPENSATION ISSUES;NON-FOOD USE OR FOOD USE HAVING ESTABLISHED TOLERANCE OR TOLERANCE EXEMPTION;

No additional payment is due at this time. If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 308-0152.

Sincerely,

Front End Processing Staff
Information Technology & Resources Management Division

Fee for Service {923037#~

This package includes the following

- (•) New Registration
- ( ) Amendment

☑ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ____

for Division

- ( ) AD
- (•) BPPD
- ( ) RD

Risk Mgr. 91

Receipt No. S- 923037

EPA File Symbol/Reg. No. 89285-R

Pin-Punch Date: 8/31/2012

☐ This item is NOT subject to FFS action.

Action Code:

Requested: B672

Granted: B672

Amount Due: $ _____

Parent/Child Decisions:

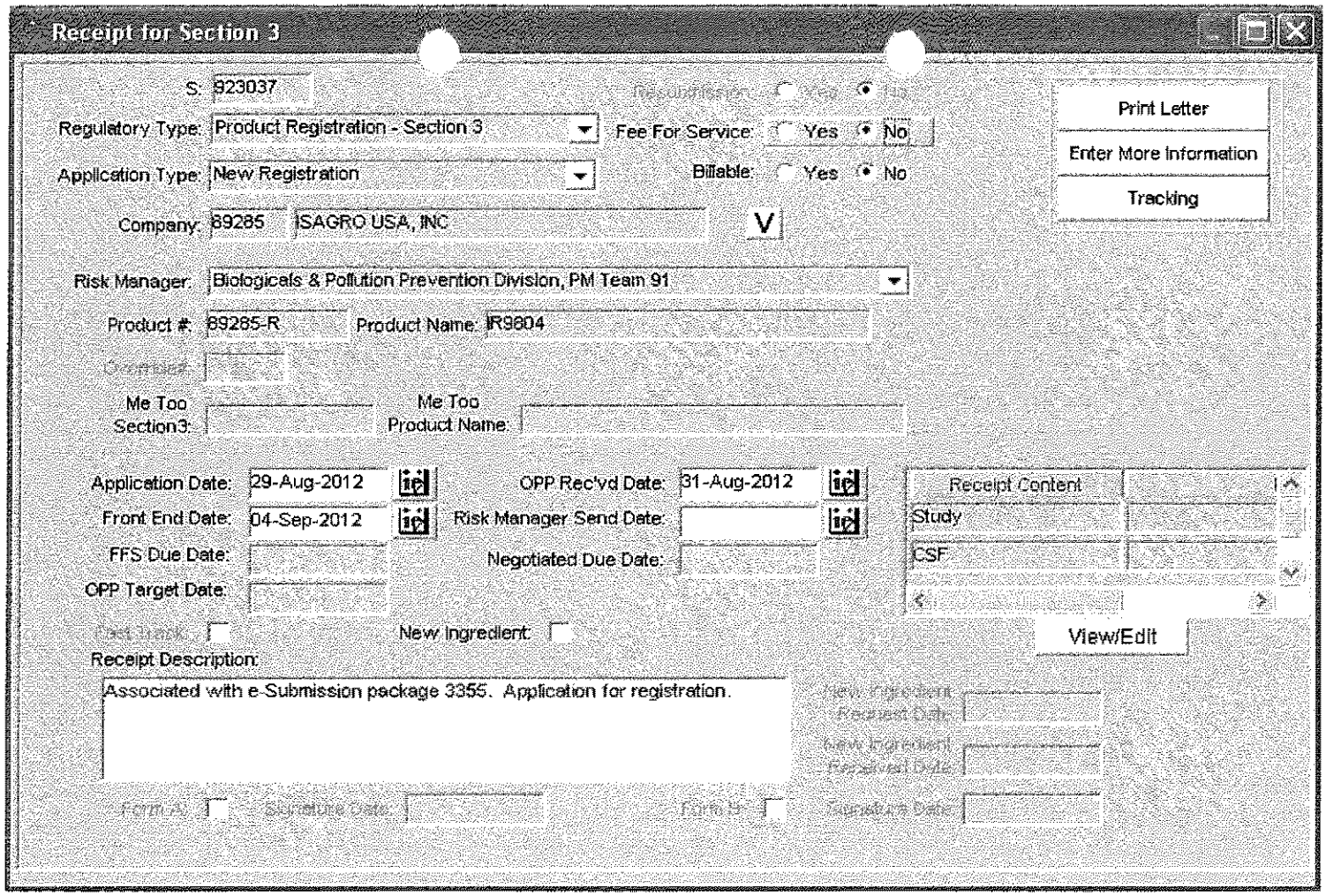
Primary: 89285-R

Secondary: 89285-E

☒ Inert Cleared for Intended Use ☒ Uncleared Inert in Product

Reviewer: Andrew Bycoland Date: 9/6/12

Remarks:


Receipt for Section 3
S: 823037
Resubmission: Yes No
Regulatory Type: Product Registration - Section 3
Fee For Service: Yes No
Application Type: New Registration
Billable: Yes No
Company: 89285 ISAGRO USA, INC
Print Letter
Enter More Information
Tracking
Risk Manager: Biologicals & Pollution Prevention Division, PM Team 91
Product #: 89285-R
Product Name: IR9804
Me Too Section3:
Me Too Product Name:
Application Date: 29-Aug-2012
OPP Rec'vd Date: 31-Aug-2012
Front End Date: 04-Sep-2012
Risk Manager Send Date:
FFS Due Date:
Negotiated Due Date:
OPP Target Date:
New Ingredient:
Receipt Content
Study
CSF
View/Edit
Receipt Description:
Associated with e-Submission package 3355. Application for registration.
Form A:
Signature Date:
Form B:
Signature Date:

Online Payment

Step 3: Confirm Payment 1 | 2 | 3

Thank you.
Your transaction has been successfully completed.

Pay.gov Tracking Information

Application Name: PRIA Service Fees
Pay.gov Tracking ID: 257QC41M
Agency Tracking ID: 74350727223
Transaction Date and Time: 08/27/2012 23:40 EDT

Payment Summary

Address Information		Account Information		Payment Information	
Account Holder Name:	Amy Plato Roberts	**Card Type:**	American Express	**Payment Amount:**	$8,269.00
Billing Address:	1150 18th Street NW, Suite 1000	**Card Number:**	**********2368	**Transaction Date and Time:**	08/27/2012 23:40 EDT
Billing Address 2:	Technology Sciences Group Inc.	**Decision Number:**			
City:	Washington	**Registration Number:**	89285-R		
State / Province:	DC	**Company Name:**	Isagro USA		
Zip / Postal Code:	20036	**Company Number:**	89285		
Country:	USA	**Action Code:**	B672		

Please read instructions on reverse side before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA	United States Environmental Protection Agency Washington, DC 20460	☒ Registration ☐ Amendment ☐ Other	OPP Identifier Number

Application for Pesticide – Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
89285-R	**Linda Hollis**	☒ None ☐ Restricted
4. Company/Product (Name) **IR9804**	PM# **91/Biochemical/BPPD**	

5. Name And Address Of Applicant *(Include ZIP Code)*

Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

☐ *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section II

☐ Amendment – Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification – Explain below.
☐ Final Printed labels in response to Agency letter dated _____
☐ "Me Too" Application.
☐ Other – Explain Below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

PRIA Category B672 – New product, unregistered source. Refer to cover letter dated August 29, 2012 for details.

Pre-payment of PRIA fee: www.pay.gov Tracking ID: 257QC41M; **Agency Tracking ID:** 74350727223; **Transaction Date and Time:** Aug 27, 2012 23:40 EDT PM

Section III

1. Material This Product Will Be Packaged In:

Child Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☒ No	☐ Yes ☒ No	☐ Yes ☒ No	☒ Metal ☐ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) _____
***Certification must be submitted**	If "Yes" Unit Packaging wgt. / No. per Container	If "Yes" Unit Packaging wgt. / No. per Container	

3. Location of Net Contents Information	4. Size(S) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	40 – 168 gallons	☒ On Label ☐ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☒ Lithographed ☐ Pager glued ☐ Stenciled ☐ Other _____

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Mel Graben / mgraben@isagro-usa.com	**Regulatory Manager**	**(919) 321-5203**

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature	3. Title	4. Typed Name	5. Date
	**Regulatory Consultant / aroberts@tsgusa.com**	**Amy Plato Roberts**	**August 29, 2012**

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete

Technology Sciences Group Inc.

712 Fifth St., Suite A
Davis, CA 95616
Direct in CA: (530) 757-1432
Direct in DC: (202) 828-8964
Fax: (530) 757-1299
E-Mail: aroberts@tsgusa.com

Amy Plato Roberts
Senior Regulatory Consultant

Linda Hollis, Chief, Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511P)
Office of Pesticide Programs, EPA
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

August 29, 2012

RE: IR9804 (EPA File Symbol 89285-R)
B672 Application for new product, unregistered source

Dear Ms. Hollis:

Enclosed with this letter you will find the following in support of a new technical grade active ingredient product, with an unregistered source:

1) Application form;
2) Copy of PRIA fee prepayment;
3) Copy of letter of meeting minutes from May 24, 2011 and Agency letter of concurrence dated July 6, 2011;
4) Confidential Statement of Formula;
5) Certification with Respect to Citation of Data form;
6) Data Matrix, including a publicly releasable "blacked-out" version;
7) Copy of Product Safety Labs letter regarding inability to conduct an eye irritation study;
8) Five (5) copies of the product label;
9) Data Volumes 1 through 9 – refer to the Transmittal Document for a complete listing of data volume titles and corresponding OCSPP Guideline Numbers.

Please note the following with regards to this application:

Identity of the Product

IR9804, containing the biochemical active ingredient **allyl isothiocyanate (AITC)**, is a Technical Grade Active Ingredient (TGAI) that is intended for further formulation into EPA-registered end-use products that will be regulated by BPPD. Intended use in formulated end-use products is as a pre-plant soil treatment for the control of soil borne fungi, nematodes, weeds and insects. End-use products will be soil-applied only, as a

pre-plant shank injection, broadcast/flat fume application, or raised bed application either shank injected into the row or injected through the drip irrigation system to field or greenhouse soils. All applications will be prior to planting crops, so this is a non-food use pesticide product.

Product Chemistry Data

A complete set of product chemistry data for a TGAI/MUP is submitted with this application – refer to Volume 2 of this submission. In addition, data on analysis of samples (five batches) is included in a separate data volume – refer to Volume 3 of this submission.

Human Health Toxicity Data

Product specific data on acute toxicity was generated as follows:

Guideline No.	Study	Result
870.1100	Acute Oral Toxicity	LD_{50} 425.4 mg/kg (Tox Cat II)
870.1200	Acute Dermal Toxicity	LD_{50}>200 mg/kg (Tox Cat II)
870.1300	Acute Inhalation Toxicity	LC_{50} >0.21 mg/L (Tox Cat II)
870.2500	Primary Dermal Irritation	Corrosive to skin (Tox Cat I)
870.2600	Dermal Skin Sensitization	Sensitizer

Based on the results of the Primary Dermal Irritation study, the test facility determined it was not necessary to conduct a Primary Eye Irritation study, as the results would be corrosive (Tox Cat I) as well. See attached letter from Product Safety Labs.

Rationales for relying on available data have been made for other Tier 1 biochemical TGAI data requirements. Rationales are based on information in published literature that provides end-points for AITC for subchronic toxicity, prenatal developmental toxicity and mutagenicity. Refer to Volume 9 of this submission.

Ecotoxicity Data

Rationales for no further testing have been submitted for all ecotoxicity data requirements – refer to Volume 9 of this submission. Rationales are based on information in published literature that provides end-points for AITC for certain nontarget species and a discussion on the anticipated lack of exposure from the methods of application and the degradation of the active ingredient post-application.

E-Dossier Submission Pilot

With the assistance of ITRMD (Bob Schultz) this label amendment and related tolerance exemption petition are being submitted electronically through the e-Dossier Submission Pilot. If you have any difficulty with the electronic submission of the information, please do not hesitate to let me know.

With this application we believe all biochemical pesticide Tier 1 data requirements for new product have been fulfilled. Let me know if there are any questions or comments.

Regards,

Amy Plato Roberts
Regulatory Consultant for Isagro USA Inc.
Direct dial (530) 757-1432; aroberts@tsgusa.com

VOLUME 1 OF 9 OF SUBMISSION

TRANSMITTAL DOCUMENT

NAME AND ADDRESS OF SUBMITTER:

Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

REGULATORY ACTION:

PRIA B672 Application for Registration of **IR9804 (EPA File Symbol 89285-R)**

TRANSMITTAL DATE:

August 29, 2012

LIST OF SUBMITTED STUDIES:

MRID NUMBER	VOLUME NUMBER	EPA STUDY TITLE	OCSPP GUIDELINE NUMBER
488241-00	1 of 9	(Transmittal Document)	----------
488241-01	2 of 9	Product Chemistry for IR9804	880.1100-1400 830.1700-1800 830.6302-7300
488241-02	3 of 9	Five Batch Analysis for IR9804	880.1700-1800
488241-03	4 of 9	IR9804 Acute Oral Toxicity Up and Down Procedure in Rats	870.1100
488241-04	5 of 9	IR9804 Acute Dermal Toxicity Study in Rats	870.1200
488241-05	6 of 9	IR9804 Acute Inhalation Toxicity in Rats	870.1300
488241-06	7 of 9	IR9804 Primary Skin Irritation Study in Rabbits	870.2500
488241-07	8 of 9	IR9804 Local Lymph Node Assay (LLNA) in Mice	870.2600
488241-08	9 of 9	Response to Tier 1 Biochemical Data Requirements for IR9804	see title page

COMPANY NAME: Isagro USA, Inc.

COMPANY OFFICIAL: 

Amy Plato Roberts, Regulatory Agent

COMPANY CONTACT: Amy Plato Roberts
Technology Sciences Group Inc.
712 Fifth Street, Suite A, Davis, CA 95616
Tel. (530) 757-1432; email: aroberts@tsgusa.com

Form Approved OMB Nos. 2070-0060; 2070-0107;2070-0122; 2070-0154

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 1.25 hours per response for registration and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, Collection Strategies Division (2137T), U.S. Environmental Protection Agency, 1200 Pennsylvania Avenue, N.W., Washington, DC 20460. Do not send the completed form to this address.

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Isagro USA, Inc. **430 Davis Drive, Suite 240** **Morrisville, NC 27560**	**82985-R**
Active Ingredient(s) and/or representative test compound(s) **Allyl isothiocyanate**	Date **August 29, 2012**
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) **Manufacturing Use**	Product Name **IR9804**

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☒ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
	**August 29, 2012**	**Amy Plato Roberts, Regulatory Consultant**

EPA Form 8570-34 (12-2003) Electronic and Paper versions available. Submit only Paper version

Form Approved OMB No, 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W. WASHINGTON, D.C. 20460

DATA MATRIX

Date	EPA Reg. No./File Symbol	Page
August 29, 2012	89285-R	1 of 4

Applicant's/Registrant Name and Address
Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

Product
IR9804

Ingredient Allyl isothiocyanate

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OCSPP 880.1100	Product Identity and Composition	488241-01	Isagro USA, Inc.	OWN	
OCSPP 880.1200	Description of Starting Materials, Production and Formulation Processes	488241-01	Isagro USA, Inc.	OWN	
OCSPP 880.1400	Discussion of the Formation of Impurities	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.1700	Preliminary Analysis	488241-02	Isagro USA, Inc.	OWN	
OCSPP 830.1750	Certified Limits	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.1800	Enforcement Analytical Method	488241-01 488241-02	Isagro USA, Inc.	OWN	
OCSPP 830.6302	Color	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.6303	Physical State	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.6304	Odor	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.6313	Stability at Normal and Elevated Temperatures, Metals and Metal Ions	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.6315	Flammability	488241-01	Isagro USA, Inc.	OWN	

Signature	Name and Title	Date
	Amy Plato Roberts, Regulatory Agent	August 29, 2012

Form Approved OMB No, 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W. WASHINGTON, D.C. 20460

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Applicant's/Registrant Name and Address	Product
Isagro USA, Inc. 430 Davis Drive, Suite 240 Morrisville, NC 27560	**IR9804**

Ingredient Allyl isothiocyanate

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OCSPP 830.6317	Storage Stability	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.6319	Miscibility	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.6320	Corrosion Characteristics	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7000	PH	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7050	UV/Visible Light Absorption	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7100	Viscosity	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7200	Melting Point / Melting Range	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7220	Boiling Point / Boiling Range	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7300	Bulk Density	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7520	Particle Size, Fiber Length and Diameter Distribution	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7550, 7560, 7570	Partition Coefficient (n-Octanol/Water)	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7840	Water Solubility	488241-01	Isagro USA, Inc.	OWN	
OCSPP 830.7950	Vapor Pressure	488241-01	Isagro USA, Inc.	OWN	

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Applicant's/Registrant Name and Address
Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

Product
IR9804

Ingredient Allyl isothiocyanate

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OCSPP 870.1100	Acute Oral Toxicity	488241-03	Isagro USA, Inc.	OWN	
OCSPP 870.1200	Acute Dermal Toxicity	488241-04	Isagro USA, Inc.	OWN	
OCSPP 870.1300	Acute Inhalation Toxicity	488241-05	Isagro USA, Inc.	OWN	
OCSPP 870.2400	Primary Eye Irritation	488241-08	Isagro USA, Inc.	OWN	
OCSPP 870.2500	Primary Dermal Irritation	488241-06	Isagro USA, Inc.	OWN	
OCSPP 870.2600	Dermal Sensitization	488241-07	Isagro USA, Inc.	OWN	
OCSPP 870.3100	90-Day Oral	488241-08	Isagro USA, Inc.	OWN	
OCSPP 870.3250	90-Day Dermal	488241-08	Isagro USA, Inc.	OWN	
OCSPP 870.3465	90-Day Inhalation	488241-08	Isagro USA, Inc.	OWN	
OCSPP 870.3700	Prenatal Developmental	488241-08	Isagro USA, Inc.	OWN	
OCSPP 870.5100	Bacterial Reverse Mutation Test	488241-08	Isagro USA, Inc.	OWN	
OCSPP 870.5300, 5375	In vitro Mammalian Cell Assay	488241-08	Isagro USA, Inc.	OWN	

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Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

Product
IR9804

Ingredient Allyl isothiocyanate

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OCSPP 850.2100	Avian Acute Oral Toxicity	488241-08	Isagro USA, Inc.	OWN	
OCSPP 850.2200	Avian Dietary Toxicity	488241-08	Isagro USA, Inc.	OWN	
OCSPP 850.1075	Fish Acute Toxicity	488241-08	Isagro USA, Inc.	OWN	
OCSPP 850.1010	Aquatic Invertebrate Acute Toxicity	488241-08	Isagro USA, Inc.	OWN	
OCSPP 850.4100	Terrestrial Plant Toxicity, Seedling Emergence	488241-08	Isagro USA, Inc.	OWN	
OCSPP 850.4150	Terrestrial Plant Toxicity,Vegetative Vigor	488241-08	Isagro USA, Inc.	OWN	
OCSPP 880.4350	Nontarget Insect Testing	488241-08	Isagro USA, Inc.	OWN	

Signature

Name and Title
Amy Plato Roberts, Regulatory Agent

Date
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430 Davis Drive, Suite 240
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Product
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Ingredient Allyl isothiocyanate

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			Isagro USA, Inc.	OWN	
			Isagro USA, Inc.	OWN	
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Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
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	Amy Plato Roberts, Regulatory Agent	August 29, 2012

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Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
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430 Davis Drive, Suite 240
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Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			Isagro USA, Inc.	OWN	
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			Isagro USA, Inc.	OWN	
			Isagro USA, Inc.	OWN	
			Isagro USA, Inc.	OWN	

Signature

Name and Title
Amy Plato Roberts, Regulatory Agent

Date
August 29, 2012

Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560
Phone (919) 321-5200
Fax (919) 321-5220

May 24, 2011

Leonard Cole,
RAL, Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511P)
Office of Pesticide Programs, EPA
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

RE: Notes on May 19, 2011 Meeting with Isagro USA Regarding AITC

Dear Mr. Cole:

The purpose of this letter is to capture the highlights of our discussions on May 19, 2011 regarding a new product registration for Ally isothiocyanate (AITC). In attendance at that meeting were:

Andre Bryceland, BPPD
Leonard Cole, BPPD
Angela Gonzales, BPPD
Linda Hollis, BPPD
Mike McDavit, BPPD
Jacob Moore, BPPD
Chris Pfeifer, BPPD

Mel Graben, Isagro USA
Dennis Krass, Isagro USA
Amy Roberts, TSG

The purpose of the meeting was to address specific questions regarding an application for registration of AITC (per the agenda for that meeting; copy attached). The group discussed the following:

- A synthetic source of AITC will be used. EPA recommending that information to confirm it is structurally similar or identical to naturally-occurring AITC should be included in the product chemistry. Isagro USA identified synthetic AITC as approximately 99% pure (specific manufacturing location and 5 batch analysis have not yet been completed) and has the same CAS No., and thus the same PC Code for EPA, as naturally-occurring AITC.

- EPA recommended taking care in addressing physical / chemical property requirements for which there are not test notes – stability, storage stability and UV/Visible Absorption.

- Isagro USA identified it will conduct an acute six-pack on the technical grade active ingredient (approx. 99%). EPA identified that information could be used to support rationales for not conducting studies on the formulated end-use product (approx. 96% AITC + [redacted]

- For compliance with the National Organic Program (NOP) for organic production (PRN 2003-1), it will be important to demonstrate that the synthetic source is the same as the naturally-occurring source – in its structure and any other ways. EPA recommended petitioning the National Organic Standards Board (NOSB) for acceptance of the synthetic source. Another path would be to make an argument to EPA and EPA will then consult with NOP/NOSB for concurrence. Either way, this should be accomplished on a separate track from the PRIA application.

- Isagro USA discussed known half-life of AITC in water and soil from published literature, and information to support rationales for ecotoxicity data requirements. The Agency indicated there would not be a concern for avian, nontarget plant and nontarget insects based on the methods of application (direct soil injection or drip tape covered in plastic) and timing of application (pre-plant, so no blooming crops or growing plants present); however, there could be a concern for runoff for aquatic species. Care should be taken in the rationales to discuss the potential for runoff into waters and effects to aquatic species.

- The Agency questioned whether or not the pre-plant application would be a food use – would there still be AITC present at the time crops are planted? It will be important for Isagro USA to provide information on why it is not a food use; specifically information on soil degradation, biodegradability, breakdown products, uptake of AITC, and/or other information to demonstrate AITC is not present or available when crops are planted. The registrant may consider risk mitigation language on the label in the form of a label restriction on when crops can be planted after treatment to ensure there is no AITC present.

  The Agency recommended BPPD scientist Mike Rexrode be included on the meeting minutes to obtain his feedback on the above issue.

- The Agency recommended submitting rationales for data requirements instead of a CITE-ALL. It is not clear if the data in EPA's files would be relevant to the product proposed.

- Isagro USA confirmed the end-use product will be marketed as a methyl bromide replacement.

- The Agency confirmed a PRIA Action Code of B672. If there are two applications (a technical and an end-use product), they will be considered a primary/secondary and as such have a full fee for the first application and a 75% fee reduction for the second (per http://www.epa.gov/pesticides/fees/related-apps.html).

Inert ingredient information may be entitled to confidential treatment

We believe the above represents the results of our discussions. If you have any questions, comments or disagree with the notes above, please do not hesitate to contact me.

Sincerely,

Mel Graben
Regulatory and Technical Manager
Isagro, USA
430 Davis Drive
Suite 240
Morrisville, NC 27560
e-mail: mgraben@isagro-usa.com
Tel: 919-321-5203
Fax: 919-321-5220

cc: Linda Hollis, Branch Chief, BPPD
Mike Rexrode, Scientist, BPPD
Russell Jones, Senior Scientist, BPPD

Product Safety Labs

Wednesday, February 08, 2012

Mel Graben
Isagro USA
430 Davis Dr., Suite 240
Morrisville, NC 27560

RE: Cancellation of Eye Irritation Study on "IR9804"

Dear Mel:

Due to the severity of results (corrosive to the skin) in the Skin Irritation Study 33711, we would suggest that you not conduct the eye irritation study and consider the sample severely irritating/corrosive to the eye. The regulations for eye irritation testing state that the study is not necessary if severe irritation is noted during skin irritation testing for the product.

Please sign below and return this page to us via fax if you agree to cancel this study.

Mel Graben

2/16/12
Date

Sincerely,

Jennifer Durando
Study Director
Product Safety Labs (www.productsafetylabs.com)
2394 US Highway 130 Suite E
Dayton, NJ 08810 USA
732-438-5100 Ext. 1536
JenniferDurando@productsafetylabs.com

IR9804

Soil Treatment Pesticide for Formulating Purposes Only

ACTIVE INGREDIENT :
Allyl isothiocyanate (CAS No. 57-06-7)* 99.8%
OTHER INGREDIENTS : 0.2%
TOTAL: 100.0%
*This product contains 8.5 lbs. active ingredient per gallon.

KEEP OUT OF REACH OF CHILDREN
DANGER — PELIGRO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label find someone to explain it to you in detail.)

FIRST AID	
IF INHALED	· Move person to fresh air. · If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth, if possible. · Call a poison control center or doctor for further treatment advice.
IF IN EYES	· Hold eye open and rinse slowly and gently with water for 15 to 20 minutes. · Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. · Call a poison control center or doctor for treatment advice.
IF ON SKIN OR CLOTHING	· Take off contaminated clothing. · Rinse skin immediately with plenty of water for 15 to 20 minutes. · Call a poison control center or doctor for treatment advice.
IF SWALLOWED	· Call a poison control center or doctor immediately for treatment advice. · Have person sip a glass of water if able to swallow. · Do not induce vomiting unless told to do so by a poison control center or doctor. · Do not give anything by mouth to an unconscious person.
NOTE TO PHYSICIAN: Because rapid absorption may occur through lungs if product is aspirated and cause systemic effects, the decision to induce vomiting or not should be made by a physician.	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. **For Chemical Emergency** **Spill Leak Fire Exposure or Accident** **Call CHEMTREC Day or Night** **Domestic North America 800-424-9300** **International 703-527-3883 (collect calls accepted)**	

EPA Registration No.: (pending as File Symbol 89285-R)
EPA Establishment No.: XXXXXX

NET CONTENTS:

Isagro USA, Inc.
430 Davis Drive, Suite 240, Morrisville, NC 27560

PRECAUTIONARY STATEMENTS
HAZARD TO HUMANS AND DOMESTIC ANIMALS

DANGER – PELIGRO. May be fatal if swallowed, absorbed through skin, or inhaled. Do not get in eyes, on skin or on clothing. Do not breathe vapour. **Corrosive.** Causes irreversible eye damage and skin burns. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wear protective clothing, chemical-resistant gloves, respiratory protection and protective eyewear. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco, or using the toilet. Remove and wash contaminated clothing before reuse.

ENVIRONMENTAL HAZARDS

Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying local sewage treatment plant authority. For guidance contact your local State Water Board or Regional Office of the EPA. Do not contaminate water when disposing of equipment washwaters or rinsate.

DIRECTION FOR USE

It is violation of Federal law to use this product in a manner inconsistent with its labelling. Read entire label. This product should be used only for formulation into a soil pesticide product for control of fungi, insects, nematodes and weeds.

This product may be used to formulate products for any additional use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s).

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

PESTICIDE STORAGE: Store unused product in original container only in cool, dry area out of reach of children and animals.

PESTICIDE DISPOSAL: Wastes resulting from the use of this product must be disposed of on site or at an approved waste disposal facility.

CONTAINER DISPOSAL for non-refillable containers: Non-refillable container. Do not reuse or refill this container. Triple rinse (or equivalent) promptly after emptying. Triple rinse as follows: Empty the remaining contents into application equipment or a mix tank. Fill the container ¼ full with water. Replace and tighten closures. Tip container on its side and roll it back and forth, ensuring at least one complete revolution, for 30 seconds. Stand the container on its end and tip it back and forth several times. Turn the container over onto its other end and tip it back and forth several times. Empty the rinsate into application equipment or a mix tank or store rinsate for later use or disposal. Repeat this procedure two more times. Then offer for recycling or reconditioning, or puncture and dispose of in sanitary landfill, or incineration. Do not bum, unless allowed by state and local ordinances.

CONTAINER DISPOSAL for rigid, refillable containers: Refillable container. Refill this container with IRF135 pesticide only. Do not reuse this container for any other purpose. Cleaning the container before final disposal is the responsibility of the person disposing of the container. Cleaning before refilling is the responsibility of the refiller. To clean the container before final disposal, empty the remaining contents from this container into application equipment or mix tank. Fill the container about 10 percent full with water. Agitate vigorously or recirculate water with the pump for 2 minutes. Pour or pump rinsate into application equipment or rinsate collection system. Repeat this rinsing procedure two more times.

LIMITATION OF WARRANTY AND LIABILITY

Read the entire label before using this product, including this Limitation of Warranty and Liability. If the terms are not acceptable, return the product at once unopened for a refund of the purchase price. This Company warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes set forth in the Directions for Use when used in accordance with the Directions for Use under normal conditions. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, ISAGRO MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY OR ANY OTHER EXPRESS OR IMPLIED WARRANTY.

FOR OFFICIAL USE ONLY

FILE SYMBOL	
REGISTRATION NO.	89285-R

CONFIDENTIAL STATEMENT OF FORMULA ENCLOSED

DATE SUBMITTED	SUBMITTED BY (✓)	
	APPLICANT	BASIC SUPPLIER
AUG 31 2012		

Do Not Write Comments, Formula, or Parts of Formula on This Envelope

NOTE

It shall be unlawful—for any person to use for his own advantage or to reveal, other than to the Secretary, or officials or employees of the United States Department of Agriculture or other Federal agencies, or to the courts in response to a subpoena, or to physicians, and in emergencies to pharmacists and other qualified persons, for use in the preparation of antidotes, in accordance with such directions as the Secretary may prescribe, any information relative to formulas of products acquired by authority of Section 4 of the "Federal Insecticide, Fungicide, and Rodenticide Act."

PR FORM 9-11
(MARCH 2006)

USDA-AI

Pages 113-114 - *Confidential Statements of Formula may be entitled to confidential treatment*